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A. M. A.
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1. Fazekas, J.F., et al.: J.A.M.A. 161:46 (May 5) 1956.
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3. Mitchell, E.H.: J.A.M.A. 161:44 (May 5) 1956.

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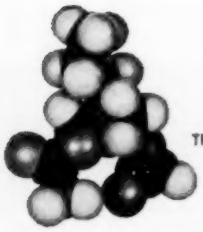

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Section on NEUROLOGY

Neurologic Manifestations of Tumors of the Glomus Jugulare

Chemodectoma, Nonchromaffin Paraganglioma or Carotid-Body-like Tumor

ROBERT G. SIEKERT, M.D., Rochester, Minn.

The tissue comprising the glomus jugulare lies in the adventitia of the dome of the jugular bulb, as well as within the temporal bone. Because of its position, tumors arising in the glomus jugulare may produce neurologic symptoms and signs. Since progressive deafness and aural discharge are the commonest symptoms associated with tumors of this structure, otologists have been primarily concerned with such lesions. Although neurologic abnormalities other than deafness frequently occur in patients with this lesion, and, in fact, neurologic manifestations may be the presenting ones, little attention has been directed in the neurologic literature to this aspect of the problem. Some authors have commented on the involvement of homolateral cranial nerves adjacent to the eighth; yet no large series of cases has been reported from this viewpoint in so far as could be determined.

The present study is concerned with 33 patients who had tumors of the glomus jugulare or related formations in this region, the neurologic signs and symptoms presented by these patients, and the concept that the varied clinical features manifested depend, at least in part, on which of the several glomic formations becomes enlarged.

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From the Section of Neurology, Mayo Clinic and Mayo Foundation. The Mayo Foundation, Rochester, Minn., is a part of the Graduate School of the University of Minnesota.

Anatomy

Guild,[1] in 1941, was the first to report clearly on the presence of the glomus jugulare. Lattes and Waltner [2] and subsequent writers stated that Valentin* had described, in 1840, a structure, "gangliolum tympanicum," resembling a ganglion and associated with the tympanic branch of the glossopharyngeal nerve, and that Krause † decided, in 1878, that this structure was not a ganglion but vascular tissue resembling the carotid body and called it "die Glandula tympanica." Watzka [3] concluded from his studies that this structure, repeatedly mentioned in anatomic handbooks, did not exist. Guild,[4] in 1953, commented that Valentin did clearly describe ganglion cells, which are frequently encountered along Jacobson's nerve (tympanic branch of the glossopharyngeal nerve), and that the tissue observed and illustrated by Krause ‡ was only the usual connective tissue in the canaliculus tympanicus. Guild thus agreed with Watzka that the tissues observed by Valentin and Krause were not glands.

According to Guild, the glomus jugulare

* Valentin, G., cited by Guild.[4]

† Krause, W., cited by Lattes and Waltner.[2]

‡ Krause, W., cited by Guild.[4]

consists usually of a flattened ovoid body about 0.5 by 0.25 mm., lying in the adventitia of the dome of the jugular bulb, immediately below the bony floor of the middle ear and near the ramus tympanicus of the glossopharyngeal nerve. He noted smaller similar bodies along the course of this branch of the glossopharyngeal nerve. Lundgren [5] suggested that these latter formations be called the "tympanic body," or "glomus tympanicum."

Guild [1] observed the similarity of the glomus jugulare and the carotid body with regard to microscopic appearance, blood supply (inferior tympanic branch of the ascending pharyngeal artery), and innervation (glossopharyngeal nerve). He suggested, too, a similarity of function, that of chemoreception. "Microscopically," he stated, "each glomus . . . consists of blood vessels of capillary or precapillary caliber with numerous epithelioid cells between the vessels."

In 1953, Guild [4] greatly amplified his earlier report. In a series of 44 pairs of temporal bones, he noted an average of slightly less than three glomera per ear and pointed out that in none of the locations in which a glomus jugulare may be present was the structure of constant occurrence. He observed these bodies with almost equal frequency along the courses of the tympanic branch of the glossopharyngeal nerve and of the nerve of Arnold (auricular branch of the vagus). More than half of the glomic formations observed in his series were in the adventitia of the dome of the jugular bulb, along the portions of these nerves that lie in the jugular fossa. About a fourth of the ears had a glomic formation associated with the tympanic plexus at the cochlear promontory. Such formations were noted throughout the courses of these nerves even as far peripherally along the tympanic branch of the glossopharyngeal nerve as the place where it becomes continuous with the lesser superficial petrosal nerve and along the auricular branch of the vagus as far as the descending facial canal. A few also were noted close to the origins of these nerves. In the instance of the latter nerve, several were so near the ganglionic region of the vagus as to be termed "juxtavagal."

It was Guild's impression that, although a glomus may lie on the auricular branch of the vagus, the innervation is originally from the glossopharyngeal nerve, carried through the auricular branch of the vagus.

Guild noted that race, sex, or laterality was not significantly related to the distribution of these glomera. They appeared to be commonest in midadult life.

Birrell [6] observed and described such tissue in the jugular ganglion (superior ganglion) of the vagus and suggested the term "jugular body" for all such formations in this region. Muratori [7] described the "paragangli intravagali" in certain birds, while White,[8] Lattes,[9] and Burman [10] have written on this "vagal body" in human beings, which lies on or within the perineurium of the ganglion nodosum (inferior ganglion) of the vagus. Thus, these formations along the course of the vagus in this region may correspond to what Guild and others have termed "juxtavagal." Similar bodies may also be seen more inferiorly along the vagus, as stated by Hollinshead in a personal communication.

Kohn [11] expressed the view that the carotid body was related to the sympathetic nervous system, at least in origin, and was thus part of the "chromaffin" system, as he preferred to call it.[12] He proposed the term "paraganglia" for the carotid and aortic bodies[13]; however, doubt has been cast on this theory, and even today the histogenesis of the carotid body and other tissue of like microscopic appearance remains in doubt.

The term "paraganglion" has remained in use despite considerable evidence that these vascular tufts are not related to the sympathetic nervous system, not the least of which is the fact that they do not give a

true chromaffin reaction.§ Likewise inaccurately, the term "paraganglion" has been attached to the glomus jugulare. Hollinshead [14] reviewed this problem in 1940 and concluded that the carotid and aortic bodies are sensory in function, and not effector, like the adrenal medulla, and that they probably represent receptors sensitive to chemical changes in the blood. In 1940, too, Schmidt and Comroe [15] reviewed their experiments which demonstrated that the function of the carotid body is chemoreception. Although described, or redescribed, later, the glomus jugulare has a microscopic appearance similar to that of the carotid body, and thus a similar function has been assumed for it. Although no experimental evidence has been advanced to support this assumption, Huppler and his colleagues [16] described a patient with a tumor of the glomus jugulare who felt dizzy and had marked rotatory nystagmus after minimal hyperventilation, both symptoms ceasing after roentgen therapy; this observation suggested to these authors that the tumor may have had physiologic function.

The definitive description, including variations of these structures in the temporal and occipital bones and elsewhere in the body, apparently has not yet been made. For the present, the term "glomus jugulare," or the term "jugular body," appears to be appropriate for all the small glomic formations in this region. In the present paper, the term "glomus jugulare" will be used, and it will connote the complex of glomera in the region of the middle ear and jugular fossa.

Pathology

In 1945, Rosenwasser [17] described a tumor that filled the cavity of the middle ear, and, although its microscopic appearance was that of a tumor of the carotid body, there was no demonstrable involvement of the carotid body. He mentioned Guild's report and noted that it provided a morphologic basis for the presence of such a lesion in that location. Since then numerous reports have appeared describing either cases newly recognized or old ones restudied with this new knowledge. Huppler and his colleagues [16] stated that somewhat more than 100 cases had been recorded at the time of their presentation in 1955.

Winship and associates [18] had noted that certain primary tumors of the middle ear had been designated as endotheliomas or hemangioendotheliomas, often by exclusion. Some of these were undoubtedly tumors of the glomus jugulare. In fact, Capps [19] commented that two cases which he had reported as cases of hemangioendothelioma proved later to be instances of tumor of the glomus jugulare. These tumors have been previously called also "granulation tissue," "simple polyps," "hemangioma," "hemangioblastoma," "hemangio-endothelioma," "hemangiosarcoma," "angiomatous granulation tissue," and "endothelioma."

Lattes and Waltner [2] suggested that these tumors be designated as nonchromaffin paragangliomas of the middle ear. However, since the derivation and function of the glomus jugulare, as well as the other bodies (aortic and carotid) of this same microscopic appearance, are probably different from those of the sympathetic system, LeCompte [20] suggested the noncommittal term "tumor of the glomus jugulare," which is used herein.

Mulligan [21] proposed the term "chemodectoma" for the histologically similar tumors of all chemoreceptor organs, and Gaffney [22] suggested "receptoma."

Grossly the tumor usually presents as a red or bluish-red polyp in the external auditory canal or behind the tympanic membrane. Because of its extreme vascularity, hemorrhage is commonly a symptom, and the tumor, which is friable, bleeds easily on manipulation, as well as spontaneously. Suppuration and granulation tissue may obscure its appearance; so that examination reveals only a red friable mass. This fact suggests that biopsy of specimens of polyps or "granulation tissue" should be generous.

§ de Castro, F., cited by Albernaz and Bucy.

The tumors are made up of nests of epithelioid cells bordered or surrounded by a stroma containing capillaries. The capillaries in the fibrous septa are constant, although stains for reticulum may have to be used to demonstrate them clearly. The cells tend to be uniform and large; the nuclei, small and variable in size and shape; the cytoplasm may be vacuolated. Mitotic figures have been observed only very rarely.

LeCompte,[20] in his fascicle, stated that these tumors are histologically indistinguishable from tumors of the carotid body. The latter he divided into three groups on the basis of microscopic appearance: (1) the usual, or commonest, type, in which the normal structure is reproduced faithfully; (2) the adenoma-like type, in which the chief cells are plump and rounded, with abundant cytoplasm resembling epithelium and supported by scanty stroma, and (3) the angioma-like type, in which the chief cells have a spindle or crescent shape, simulating endothelial cells. Despite these differences, the fundamental pattern, particularly that exhibited on use of stains for reticulum, is the same.

The extent of the lesion at necropsy varies, as might be expected. Widespread involvement has been observed, particularly in those cases in which neurologic abnormalities were present. Henson and associates[23] described a specimen in which the tumor extended from the pterygoid fossa, anteriorly, and to the atlanto-occipital joint, posteriorly; laterally, it involved the middle ear and mastoid, and, medially, it was bounded by the fifth and seventh cranial nerves. Nodular masses were seen in the dura over the posterior aspect of the petrous bone. In this case, and in others, a tongue of tumor tissue extended for a variable distance down the lumen of the internal jugular vein. Albernaz and Bucy[24] showed a fusiform swelling of the vagus nerve.

In general, these tumors are considered nonmalignant, although local invasion and destruction of the mastoid process, the petrous portion of the temporal bone, and the occipital bone, and extension into the cranial cavity are commonly seen. Thus, while histologically benign, they are malignant in a practical sense. Metastasis is extremely rare ‖ and has even been doubted.[22]

Multiple tumors of nonchromaffin bodies have been reported,¶ and in one review[26] tumors of the glomus jugulare and the carotid body were present in the same patient in more than 10% of the cases analyzed. This suggests a "simultaneous" response on the part of these various bodies. A familial occurrence has been reported.#

Material Studied

Thirty-three cases form the basis of this report. The diagnosis of tumor of the glomus jugulare was made microscopically in each, either at biopsy of a polyp or mass in the ear or from tissue removed at mastoidectomy or other operative procedure in this region. Two of these cases have been reported previously.* Tumors of the carotid body were not included in the study. The site of origin was assumed to be any one (or several) of the glomic formations comprising the glomus jugulare complex. One patient had only a mass presenting both below the parotid gland and in the pharynx, which on biopsy proved to have the microscopic appearance of a tumor of the glomus jugulare. This case seems to be like the case of Burman[10] and the case of Albernaz and Bucy,[24] who apparently reported simultaneously the fifth case of "vagal body tumor." In one patient, a tumor of the carotid body was observed several years after one in the glomus jugulare.

Results

Sex.—Of the 33 patients, 22 were women and 11 were men. This predominance of female patients has been noted by all reviewers, and no explanation has been found for it, although a hormonal influence has been suggested.

Laterality.—In 20 patients (14 women and 6 men) the tumor involved the left side, and in 13 (8 women and 5 men), the

‖ References 2 and 19.

¶ References 9 and 25.

Bartels, J., cited by Capps.[19]

* References 16 and 27.

right side. In the 79 cases that Bickerstaff and Howell [26] collected from the literature, a similar ratio for the sides was noted; in 62% of the cases they reviewed, the left side was involved. No reason for this is known.

Age.—The age span was considerable. At the time the diagnosis was made the ages of the patients in the present series ranged from 33 to 71 years. Six patients were in their 30's, 13 in their 40's, 8 in their 50's, 5 in their 60's, and 1 was 71. Thus, 27 of the 33 patients were between 30 and 59 years of age when the diagnosis was established.

The ages when symptoms began ranged from 2 to 65 years; however, only one patient began having symptoms before 20 years of age, and this one had an extraordinarily long history, of 42 years, of chronic purulent aural discharge. Excluding this one patient, six patients began to have symptoms in their 20's, eight in their 30's, nine in their 40's, seven in their 50's, and two in their 60's. Thus these neoplasms tend to develop in young or middle-aged adults.

The duration of symptoms before the diagnosis was established averaged seven years, and about half the patients had had symptoms from two through eight years before the diagnosis was made. No relationship was apparent in this series between age of onset of the symptoms and sex, side, or presenting symptoms. The course of these tumors tends to be long.

Symptoms.—The initial symptoms are listed in Table 1. Tinnitus, noted by 15 patients, was the commonest initial symptom. It was described almost always as an intermittent throbbing, pounding, or rushing noise, synchronous with the pulse and heard in the involved ear. Although variable in degree, it tended to be persistent. Only two patients noted a "cricket" sound, but these had no other evidence to suggest that this represented a fragment of hemifacial spasm. In four patients a bruit was audible over the mastoid process, and in one, over the tumor presenting below the parotid. Deafness was recalled by 11 as the initial complaint, and otorrhea by 8. The deafness always began insidiously and worsened gradually. Three patients noted hoarseness first, and one dysphagia as the initial symptom. All of these four also noted deafness later in their illness, and at the time of their examination the lower cranial nerves were involved. One patient noted bulging in the throat, and another fullness and pain in the ear, as the initial symptom.

TABLE 1.—*Symptoms in Thirty-Three Cases of Tumor of the Glomus Jugulare*

Symptoms	Patients*	
	Initial Symptoms	All Symptoms
Deafness	11	27
Tinnitus	15	24
Aural discharge	8	17
Vertigo or dizziness		12
Pain in ear	1	12
Hoarseness	3	7
Headache		6
Weakness of face		5
Twitching of face		2
Dysphagia	1	4
Diplopia		3
Paresthesia of tongue		3
Bulging in throat	1	2
Pain in face		1

* Several patients apparently had simultaneous onset of several symptoms.

Throughout the course of the illness various symptoms appeared (Table 1). Deafness, which was the commonest, developed in 27 patients. Tinnitus was recalled by 24 and aural discharge by 17. Seven of these latter mentioned bloody or blood-tinged discharge. The remainder had a purulent or watery discharge. Twelve patients noted vertigo or dizziness, five of whom had episodes of real (rotational) vertigo and the rest a vague unsteady or light-

headed feeling. Pain in the ear or mastoid or, more frequently, an uncomfortable "full feeling" in the ear was a complaint in 12 patients. Four of these patients had unilateral suboccipital pain on the side of the lesion, which was usually of moderate intensity, rather than severe. Other symptoms were hoarseness, generalized headache, weakness and twitching of the face, dysphagia, diplopia, paresthesia of half the tongue, bulging in the throat, and pain in the distribution of the trigeminal nerve.

It is important to note that of the symptoms complained of by these patients, all save one (aural discharge) may be considered to fall within the neurologic province, and, as will be seen, the neurologic examination disclosed more widespread involvement of the nervous system than the symptoms would suggest.

Clinical Findings.—The abnormalities found on clinical examination are listed in Table 2. All but one patient had a visible tumor mass. In 31 it was seen on otoscopic examination. In the other patient it bulged into the pharynx medially and below the parotid gland laterally as an external mass. In two patients a tumor presented both in the pharynx and in the ear. In only 3 of 14 patients was a tumor not visible at the time when gross neurologic abnormalities were already present. Subsequent examinations several years later (five, three, and two years, respectively) revealed a tumor in the external auditory canal in each of these three cases.

TABLE 2.—*Findings on Examination of Thirty-Three Cases of Tumor of the Glomus Jugulare*

	Patients
Tumor seen	32
Deafness	27
Involvement of other cranial nerves	14
3	2
5	3
6	4
7	7
9	10
10	10
11	8
12	10
Bruit over mastoid	4
Nystagmus	2
Ataxia	1
Horner's syndrome	1
Exophthalmos	1

The tumor presented in several ways: as a polyp easily visible in the external auditory canal, reddish or bluish-red, often pulsating; as a polypoid growth behind the eardrum, or reddening and obscuring the landmarks of the drum, or as a red, friable mass with the appearance of granulation tissue in the external canal. In four patients a tumor was seen within the cavity left after radical mastoidectomy. Growths of this type bleed easily, and occasionally when they are removed by simple polypectomy, brisk hemorrhage may occur.

Deafness also was a common feature and was present to varying degrees in 27 patients. Both conduction and perceptive types were seen. In those patients with deafness in whom a caloric examination of the labyrinth was carried out, depression or absence of response on the involved side was noted. Deafness was present in all 14 cases in which other neurologic involvement was observed. In only one of these patients was the eighth nerve not involved on first examination, but on later examination deafness with absence of response to caloric stimulation was noted.

Involvement of the fifth cranial nerve, observed in three patients, was manifested by diminution of cutaneous sensibility in all three divisions, as well as by weakness of the ipsilateral masticatory muscles. Four patients had palsy of the lateral rectus muscle; two had involvement of the third

cranial nerve. Six patients manifested a marked peripheral type of facial nerve palsy, and one, slight weakness. In three of these, twitching of the facial muscles not unlike that of typical or cryptogenic hemifacial spasm was observed. These three patients also had a "rushing" tinnitus synchronous with the pulse. Only Brown [28] has previously reported twitching of the facial muscles in patients with this lesion. The appearance of the hemifacial spasm from other lesions in the posterior fossa has, of course, been noted, although it is uncommon.

The 9th, 10th, 11th, and 12th cranial nerves were each involved in about a third of the cases in this series. They were usually involved together, although not invariably so. In several cases, conspicuous atrophy of the sternocleidomastoid and trapezius muscles and the tongue was noted; in cases of tongue involvement fascicular twitching was often noted.

Involvement of cranial nerves was always on the same side as the lesion; it began gradually and progressed slowly in all but one case. In the one exception, hoarseness began suddenly and was the first complaint. In the literature, also, the onset and course of the cranial nerve palsies have usually been said to be insidious and slow, although rapid, development of a lesion in the seventh nerve has been reported.† In one of the patients in the present series facial palsy developed over a period of two days and was associated with an upper respiratory infection.

A bruit was heard over the mastoid process in four patients. In each it decreased or disappeared with pressure on the homolateral carotid artery. In one other patient who had no neurologic abnormalities it was heard only over the tumor as this presented below the parotid gland. Ataxic gait and incoordination of the homolateral limbs were noted in one patient. A Horner syndrome (ipsilateral) and bilateral exophthalmos were each observed in one patient. Conspicuous nystagmus was noted in two patients on lateral gaze. The neurologic abnormalities for each patient are listed in Table 3.

† References 29 and 30.

TABLE 3.—*Neurologic Abnormalities in Fourteen Patients with Tumor of the Glomus Jugulare*

Case	Age, Yr.	Sex	Neurologic Involvement	X-Ray Findings
1	36	F	7*, 8; hemifacial spasm	Mastoid sclerosis
2	47	M	8-12	Mastoid clouding
3	55	M	3, 5, 6, 8-10, 12	Destruction of middle fossa and petrous ridge
4	34	F	5, 6, 8-12; bruit	Widening of internal auditory meatus
5	45	F	7, 8	Mastoid clouding
6	55	M	8-12; nystagmus	Destruction of petrous ridge and mastoid
7	33	F	7-12; hemifacial spasm	Destruction of petrous ridge and mastoid
8	66	F	8-12	Mastoid sclerosis
9	50	M	7, 8; bruit	Destruction of petrous tip
10	71	M	6-12; hemifacial spasm; bruit; Horner's syndrome	Mastoid clouding
11	41	M	8-10, 12	Normal
12	65	F	8-12; bruit	Mastoid sclerosis
13	52	F	7, 8; ataxia; nystagmus	Destruction of petrous ridge
14	39	F	3, 5, 6-12; exophthalmos	Destruction of mastoid

* Numbers indicate cranial nerves involved.

Mention should be made of two cases which are not included in Table 3 because the neurologic findings were questionably abnormal. One of these patients had minimal nystagmus on lateral gaze, and the other had suggestive unsteadiness in walking. The roentgenograms of the former were normal; those of the latter showed evidence of destruction of the mastoid, in addition to the changes of a previous mastoidectomy. Both patients had a tumor, easily visible on otoscopy, and ipsilateral total deafness with a dead labyrinth.

Thus, in 14 (42%) of the 33 cases of tumor of the glomus jugulare reported on here, other cranial nerves, in addition to the eighth cranial nerve, were involved. Deafness was present in 27 (82%) of the entire series of 33 cases.

Roentgenograms.—Roentgenograms of the skull and the mastoid process were normal in seven of the entire group of patients and revealed only clouding or sclerosis of the mastoid in 15 and evidence of destruction of bone in 10. Roentgenograms were not made of the patient with the "vagal body tumor." The sites of destruction were the mastoid process, petrous pyramid, the occipital bone, and the floor of the middle fossa. Seven of the 10 patients with destructive changes had evidence of involvement of the nervous system, in addition to that of the eighth nerve. Three patients had destructive changes in the mastoid or petrous tip and no neurologic involvement other than that of the acoustic nerve. The roentgenograms of 7 of the 14 patients with neurologic abnormalities in addition to those of the eighth nerve showed destructive changes in bone; roentgenograms of 6 patients showed sclerosis of the mastoid, and those of 1 patient were normal.

Course.—The earliest symptoms of 29 patients were otologic in nature (deafness, tinnitus, and otorrhea). Subsequently, neurologic abnormalities developed in 11 of these. The first neurologic abnormality was involvement of the facial nerve in 6 of these 11 patients, of the 5th and 6th nerves in 1, of the 10th and 11th in 3, and of the 6th through the 12th cranial nerves in 1. Thus, after the deafness developed in these 11 patients, the tumor extended to more rostrally placed cranial nerves in about two-thirds and to more caudally placed cranial nerves in one-third. It is of interest that an average of seven years elapsed before the development of neurologic symptoms in these 11 patients.

In two patients otologic symptoms (deafness) and neurologic abnormalities (involvement of the 9th through the 12th cranial nerve) began simultaneously.

One patient had involvement of the 5th, 6th, 9th, 10th, 11th, and 12th cranial nerves at least three years before involvement of the 7th and 8th nerves.

One of the 33 patients had neither otologic nor neurologic abnormalities but complained only of a bulging into the pharynx.

Miscellaneous Findings.—A lumbar puncture was done in one case, and the fluid was normal except for 60 mg. of protein per 100 cc. Angiography and pneumoencephalography were done in another; the carotid angiogram was normal, while the pneumoencephalogram showed questionable evidence of abnormality in the posterior fossa.

Several cases will serve to illustrate these features. Normal laboratory and noncontributory data have been eliminated.

Case 1.—A 36-year-old woman was referred to the neurologist because of a facial tic of three months' duration. Additional history revealed that she had been aware of gradual and progressive deafness and a thumping noise in the right ear for about seven years. On several occasions the right ear had been syringed and blood-tinged fluid noted. One year prior to admission numerous episodes of vertigo occurred over a period of two months. About three months before her visit the right corner of the mouth began to twitch.

Examination revealed deafness of the right ear, right hemifacial spasm with slight weakness of the right facial muscles, and a reddish polypoid mass in the right external auditory canal. No bruit was heard. Roentgenograms of the cranial vault were interpreted as normal, but slight periantral sclerosis was found in the right mastoid process. The microscopic appearance of the aural polyp was compatible with tumor of the glomus jugulare.

In this case, after progressive failure in hearing for a long period, and bleeding from the ear, hemifacial spasm developed, which occasioned the patient's referral.

Prior to this time she would have fitted into the large group of patients presenting only deafness, tinnitus, otorrhea, and a polyp in the ear.

Case 2.—For three years prior to admission, a 47-year-old man was aware of gradually failing hearing and intermittent hissing in the right ear.

Examination disclosed complete deafness on the right and absence of response of the right labyrinth to caloric stimulation. The right side of the palate and pharynx and the right vocal cord were weak. The right sternocleidomastoid and trapezius muscles and the right half of the tongue were weak and atrophied. Hypesthesia of the right half of the pharynx was noted. A reddish mass was seen pushing out the right eardrum. Roentgenograms showed only slight clouding of the right mastoid. No bruit was heard. Microscopic appearance of

the growth was compatible with a tumor of the glomus jugulare.

This patient apparently was aware only of deafness and tinnitus, but examination disclosed involvement of the last five cranial nerves.

CASE 3.—Three years before registration, a middle-aged man became aware of deafness and a sense of fullness in the right ear. Intermittently he felt a throbbing, synchronous with the pulse, in the right ear. Otologic examination was said to have shown a "shifted drum." A year later, dull frontal pain and discomfort in the ear began and, because of these symptoms and continuing progressive loss of hearing, a fenestration operation was performed. Several weeks thereafter the patient experienced diplopia, and the right eye turned inward for a few months. Loss of hearing continued to increase, tinnitus became persistent, and the pain gradually involved the entire right side of the face and forehead. For one month prior to admission, the right lid drooped, and shooting pain of brief duration occurred in the region supplied by the right trigeminal nerve, although no trigger area was noted.

Examination disclosed weakness of the right medial, superior, and lateral rectus muscles. The right lid drooped, and the right pupil was larger than its fellow. The facial muscles appeared to be normal. The muscles supplied by the right mandibular nerve were weak, and cutaneous sensation in the right side of the face was decreased. The right side of both the palate and the pharynx was weak, and sensation was blunted. In the pharyngeal recess (fossa of Rosenmüller) was a slight bulge. Slight ataxia was observed on tandem gait. There was conduction deafness on the right, and the tympanic membrane bulged from a tumor beneath it. The trapezius and sternocleidomastoid muscles appeared to be normal. The tongue protruded slightly to the right.

Roentgenograms of the skull showed erosion of the petrous portion of the temporal bone and erosion and destruction of the floor of the middle fossa. Microscopic appearance of the lesion beneath the tympanic membrane was consistent with that of tumor of the glomus jugulare.

This patient's principal and most annoying symptom was pain in the face, which had some features of tic douloureux. Deafness and tinnitus, which had commenced previously, had been followed by an unsuccessful fenestration operation and still later by diplopia. Besides the involvement of the 8th nerve, the 3d, 5th, and 6th cranial nerves were involved anteriorly, and the 10th and 12th nerves, caudally. A tumor was seen in the ear and in the pharynx.

CASE 4.—A 34-year-old woman was seen at the Clinic in 1950, at which time she stated that trouble in swallowing had begun about 16 months before. Several months later, her voice gradually became hoarse, and some pain developed in the left shoulder and arm and on the left side of the head and neck. Prickling of the left side of the tongue was present for a few months, and six months before admission diplopia on gaze to the left began. She felt dizzy and became aware of a pumping noise in her left ear. The spinal fluid was said to have been normal.

Examination disclosed involvement of the left 6th, 9th, 10th, 11th, and 12th cranial nerves. A bruit was heard over the left mastoid process. Otoscopic examination revealed normal conditions. Function of the eighth nerve was normal. There was questionable decrease in cutaneous sensation of the left side of the forehead. Roentgenograms of the skull, including Stenver's and basal views, were normal. A left internal carotid angiogram was normal; a vertebral angiogram was unsuccessful. The pneumoencephalogram was suggestive of a lesion in the posterior fossa. Operation was refused.

The patient was again seen in 1953. Examination now disclosed slight loss of hearing on the left and reddish material behind the left tympanic membrane. In addition to the palsies of the cranial nerves noted previously, she now had definite weakness of the masseter, pterygoid, and facial muscles on the left. Questionable hypesthesia was present over the left side of the face. Roentgenograms showed clouding of the left mastoid and slight widening of the left internal auditory meatus. Microscopically, the tissue removed from behind the tympanic membrane appeared compatible with tumor of the glomus jugulare.

Deafness, tinnitus, and involvement of the lower four cranial nerves were present early. Later, palsy of the sixth nerve developed. Examination demonstrated no involvement of the seventh or eighth nerve. When this patient was seen three years later, progression had occurred in the previously involved structures, and, in addition, the fifth, seventh, and eighth nerves were involved and a tumor was noted beneath the eardrum.

When gross neurologic abnormalities are present, the absence of visible tumor appears to be unusual.

Comment

The data on the series presented herein indicate that neurologic symptoms and signs are commonly present in patients with tumors of the glomus jugulare. These patients complained of such neurologic symptoms as deafness, tinnitus, dizziness, vertigo, pain in the ear or head, hoarseness, dysphagia, weakness and twitching of the face, diplopia, and pain or paresthesia in the tongue and face. There was objective evidence of involvement of the 3d, and the 6th through the 12th cranial nerves, and ataxia, nystagmus, Horner's syndrome, and exophthalmos. The acoustic nerve was involved in a total of 27 patients (82%). Such neurologic involvement exclusive of that of the eighth cranial nerve was seen in various combinations in 14 patients (42%). Roentgenograms showed destructive changes in about one-third of all the cases, and in one-half of those with neurologic abnormalities.

Other neurologic signs than those noted in the present group have been reported only infrequently. These include signs referable to the pyramidal tract,‡ papilledema,§ and prominent ipsilateral cerebellar signs.‖ The examination of cerebrospinal fluid has been done infrequently. Its pressure and protein content may be normal or elevated. The protein content apparently is usually elevated when neurologic abnormalities outside those of the eighth nerve are present, although not invariably so. Values between 100 and 200 mg. per 100 cc. may be seen, although 416 mg. per 100 cc. has been observed.[26]

Roentgenologic studies with air as the contrast medium also have been reported on infrequently. In Hierons'[32] case the patient showed evidence of a lesion of the cerebellopontine angle.

Angiograms of the carotid artery (common or internal) and of the vertebral artery may disclose normal conditions.¶ A vascular tumor has been observed in a vertebral angiogram,# and Alexander and associates[29] observed a vascular mass in the posterior fossa in an angiogram of the common carotid artery. Henson and his associates[23] suggest that the frequent failure of internal carotid and vertebral angiograms to show a tumor supports the contention that the blood supply of the tumor is from the external carotid artery.

The paucity of reports on pneumography and angiography suggests also that the diagnosis is usually made without such studies.

Only Henson, Crawford, and Cavanagh[23] and Bickerstaff and Howell[26] have been concerned with this lesion primarily from the neurologic standpoint. The former group analyzed 77 reported cases, including 6 of their own, of "tympanic and jugular glomus tumours." They noted that 31 (40%) had evidence of "intracranial extension." This is in agreement with the present series, and the types of neurologic involvement were similar, that is, a preponderance of lesions of the cranial nerves. It is of interest that all their own patients had a vascular polyp in the affected ear.

Bickerstaff and Howell analyzed 87 cases from the literature and added 3 of their own. In this collection, 58 patients (about 65%) had paralysis of one or more of the lower cranial nerves other than the eighth; 85 patients (94%) had bulging of the tympanic membrane or a polyp in the external auditory canal, while only 41 (46%) had certain involvement of the acoustic nerve, although they commented that it was probably involved in a greater number, as the reports reviewed were not always clear on this point.

‡ References 23 and 31. Bartels, J., cited by Capps.[19]

§ References 6 and 32.

‖ References 18 and 29.

¶ References 23, 28, and 33.

References 31 and 34.

Many authors have commented on the fact that the neurologic symptoms are late in developing; that is, although lesions of the eighth nerve, and later of the seventh nerve, are seen relatively early in a number of cases, the other neurologic symptoms are seen late. While in general this is true, the present study indicates that neurologic involvement may be early. The early neurologic symptoms may take the form of involvement of the seventh nerve or of structures near the jugular fossa, usually the vagus nerve. Later a jugular foramen syndrome may be seen.

The scattered distribution of the constituent bodies comprising the whole of the glomus jugulare complex may be the reason for the variability in the clinical picture. Birrell[6] and Guild[4] have commented on this, and Henson and associates[23] alluded to it, by noting that the clinical story is primarily otologic or primarily neurologic or a combination of these two types.

Bickerstaff and Howell classified these neoplasms into four main clinical types: (1) those with aural symptoms only; (2) those with neurologic involvement developing many years after aural symptoms; (3) those with neurologic and aural symptoms developing concurrently, and (4) those with neurologic symptoms appearing before aural symptoms. They stated that this variability depends on the origin of the tumor.

Henson and his co-workers apparently considered that the specific origin can always be stated, but it has seemed to other authors and to me that the actual glomus giving rise to the tumor may be hard to identify. Evidence cannot be found to show that the other glomera remain uninvolved, owing certainly, in part, to the fact that distortion of the normal anatomy has occurred. Simultaneous onset from several glomera might be a factor, for in a number of cases apparently independent tumors have involved several of these so-called nonchromaffin organs throughout the body.

Winship and Louzan[35] showed that some of these growths may arise from the tympanic body (Lundgren's term) and remain confined to the middle ear. Black[36] stated that about half of all glomus tumors in this region arise from the dome of the jugular bulb and the remainder from glomera within the temporal bone proper. Additionally, local differences may account for spread in different ways, although the glomera may be in similar, though not identical, positions.

Since, as pointed out, glomic formations in this region are to be found in various and inconstant locations, several modes of extension and appearance may occur when tumors arise from them. Thus, the first symptoms caused by a tumor of the glomus in the facial canal will not be the same as the symptoms of a growth on the cochlear promontory, or those when a tumor begins near the nerves in the jugular foramen.

Commonly, the first involvement is of the middle ear. The tumor may arise there primarily, as from the cochlear promontory, or invade from the jugular fossa, below, through the thin floor of the middle ear. This early involvement of the middle ear certainly accounts for the rather common early loss of hearing.

Once in the middle ear, the growth may continue laterally and destroy or push out the tympanic membrane, to appear in the external auditory canal, or it may extend upward into the petrous portion of the temporal bone, backward into the mastoid, medially toward the pharynx, or inferiorly into the occipital bone or into the posterior cranial fossa. Thus, a tumor arising near the jugular ganglion may be immediately within the posterior cranial fossa; that from the vagal body may project as a rounded hillock into the pharynx, or beneath the ear externally, or both. The exact site of origin may be difficult to prove.

Summary

A series of 33 patients with tumors of the glomus jugulare has been studied from the neurologic standpoint. Involvement of the acoustic nerve was observed in 27 patients; other neurologic involvement also, in 14. The neurologic symptoms of this lesion include deafness, tinnitus, vertigo, hoarseness, dysphagia, facial weakness, diplopia, and pain in the ear, head, or face. Involvement of the 3d through the 12th cranial nerves, except for the 4th, and bruit, ataxia, nystagmus, Horner's syndrome, and oxophthalmos were present.

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Symptoms in Relation to Psychiatric Diagnosis and Treatment

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Introduction

One of the points at which fundamental psychiatric knowledge seems most likely to be advanced at the present time is that of the characteristics which, within broad diagnostic groups, distinguish patients who respond favorably to treatment from those who do not. Among such characteristics, psychiatric symptoms seem worthy of careful consideration. The primary aim of this investigation was to determine whether, within the broad groups of psychoneurotic, depressive, and schizophrenic patients, those showing a good therapeutic response and those showing a poor one differed to a statistically significant degree in their psychiatric symptomatology prior to treatment. There is, of course, good reason to believe that psychiatric diagnoses are only a very approximate description of the facts and that the overlap of symptoms is extensive. A second aim of the inquiry was to discover how far the three diagnostic groups themselves differed significantly in symptoms and how great was the amount of overlap. It was also possible to obtain incidental information on relationships within and between the techniques of assessing symptoms that were employed.

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Patients and Data

The sample under investigation comprises the first 100 informal patients admitted to Fairdene Hospital since April 1, 1953. It may be noted here that during the year following April 1, 1953, a total of 529 patients of largely good prognosis were treated in Fairdene Hospital, which is outside the jurisdiction of the British Lunacy and Mental Treatment Acts. This figure includes the first 100 patients especially studied here. In another investigation, to be published elsewhere, comparisons were made as to the effects of various treatments and treatment combinations on the total sample of 529. The evidence suggested that, within each diagnostic group, the particular form of treatment applied did not significantly affect the patient's duration of stay in hospital or his status (recovered, relieved, or unimproved) at discharge. Therefore it was decided in this inquiry to consider therapeutic response irrespective of treatment applied. Another problem considered in this larger investigation was whether, within the various diagnostic groups, the psychiatrist's choice of treatment was influenced by duration of illness before admission or by the patient's age. The only significant difference was within the schizophrenic group, where those treated with electroshock treatment alone had a higher mean age than those treated with deep insulin coma alone. The diagnosis was the final opinion of the senior psychiatrist in charge of the case. This was assimilated to the International Statistical Classification[1]; patients coded 310 to 318 were taken as psychoneurotic; those coded 301.1 or 302, as depressive; those coded 300, as schizophrenic, and cases coded otherwise were omitted. Response to treatment was assessed by one of us (R.K.F.) one year after admission.

Recovered: Free from symptoms and able to resume work at the previous occupational level

Relieved: Patients exhibiting various symptoms, but able to leave hospital and resume work at or below the previous occupational level

Unimproved: Neither of foregoing levels.

The psychoneurotics numbered 23 (5 recovered, 14 relieved, 4 not improved); the depressives, 19 (7 recovered, 11 relieved, and 1 not improved), and the schizophrenics, 51 (3 recovered, 38 re-

lieved, and 10 not improved). The omitted diagnoses were psychopathies (3), organic psychoses (3), and puerperal psychoses (1). There were 40 male and 60 female patients altogether.

The assessment of symptoms was carried out according to the Wittenborn system of quantified multiple psychiatric diagnosis[2] approximately three weeks after admission by the senior psychiatrist in charge of the case. The Wittenborn system consists or rating scales for assessing the presence and severity of 55 different psychiatric symptoms; the scales have separate verbal descriptions of levels for each symptom, there usually being four levels. Before the investigation was begun, three minor changes in wording were introduced into the scales, to forestall objections. Two of these were cultural in character ("amounts of food" for "servings," in Scale 10, and "impudent in any way" for "impudent or cocky," in Scale 11); the other was to avoid a theoretical assumption (omission of "intrapsychic" from Scale 21). From the scale ratings are calculated weighted scores on nine symptom clusters, derived by factor analysis, which are denoted by the psychiatric diagnoses to which they seem most closely to correspond. The weighted cluster scores may be converted into standard scores, from which a profile may be constructed for each patient.

At approximately the same time as this psychiatric assessment, the patients provided by means of the Minnesota Multiphasic Personality Inventory another assessment of their symptoms. They were also given as tests of abilities the Wechsler-Bellevue Vocabulary and the Wesman Verbal Reasoning and Numerical Ability Tests.[3] In addition, information was secured as to the incidence of personal stresses in these patients, the findings on which are reported separately.

The data actually employed for comparison in this investigation were as follows:

1. Scores on the 3 tests of abilities
2. Ratings on the 55 Wittenborn scales
3. The 9 Wittenborn weighted cluster scores
4. Raw scores on the 13 Minnesota scales

The comparisons made were as follows:

A. Diagnosis
   1. Psychoneurotic *vs.* Depressive
   2. Psychoneurotic *vs* Schizophrenic
   3. Depressive *vs.* Schizophrenic

B. Response to Treatment
   1. Psychoneurotic Recovered *vs* Not Recovered
   2. Psychoneurotic Improved *vs.* Not Improved
   3. Depressive Recovered *vs.* Not Recovered
   4. Schizophrenic Improved *vs.* Not Improved

Not Recovered denotes Relieved plus Not Improved; Improved denotes Recovered plus Relieved. The omitted possibilities were disregarded, owing to the small frequencies involved. The statistical significance of differences was tested by "Student's" t ratio.

Results: Significant Differences

In so many comparisons a certain number would be statistically significant at the 5% and 1% levels by chance alone. In the diagnostic comparisons the number found was greatly in excess of this (240 comparisons: chance expectancy, 10 at 5% and 2 at 1% levels; actually obtained, 26 at 5% and 26 at 1% levels). In the response comparisons the excess was much less marked (320 comparisons: chance expectancy, 13 at 5% and 3 at 1% levels; actually obtained, 18 at 5% and 5 at 1% levels). This would suggest that much greater weight should be attached to the diagnostic differences. Against this it must be remarked that the major part of the comparisons were the Wittenborn scales; the decision as to diagnosis was made by the same psychiatrist who assessed these, but the decision as to response was made independently of knowledge as to the Wittenborn ratings.

The following statistically significant differences were found: Those significant at or beyond the 1% level are indicated by an asterisk. The remainder were significant only at or beyond the 5% level. Wittenborn usually denotes the scales verbally by the extreme level. In many scales this misrepresents the position, and a truer picture is given by a more general description, which we have substituted here.

1. *Diagnosis: Psychoneurotic* vs. *Depressive.*—The psychoneurotics had higher mean ratings on the following Wittenborn symptom scales:

Use made of physical disease symptoms	9
Hysterical behavior	25
Feelings of anxiety	28
Emotional factors in organic symptoms	29
Efficiency impaired by anxiety	49

2. *Diagnosis: Psychoneurotic* vs. *Schizophrenic.*—The psychoneurotices had higher mean ratings on the following Wittenborn symptom scales:

Self-blaming behavior	5
Use made of physical disease symptoms*	9
Phobias	15
Hysterical behavior	25
Feelings of anxiety*	28
Emotional factors in organic symptoms*	29
Demands for attention	31
Efficiency impaired by anxiety	49
Lack of cooperativeness	55

They also had a higher mean score on the Wittenborn Conversion Hysteria Cluster.

The schizophrenics had higher mean ratings on the following Wittenborn symptom scales:

Rapid change of ideas*	2
Unaware of the feelings of others*	8
Social withdrawal	13
Personal neglect*	16
Bizarre or obscure thinking*	24
Feelings of persecution	26
Feelings of reference or influence	27
Lack of insight*	34
Variable rate of speech	36
Failure of affect	41
Perceptual disturbances	45
Relevance of words to recognizable ideas	48
Forgetting of earlier insights	50
Circumstantial speech	51

They also had higher mean scores on the following Wittenborn Clusters:

Depressed state
Schizophrenic excitement*
Paranoid condition*
Paranoid schizophrenia*
Hebephrenic schizophrenia*

3. *Diagnosis: Depressive* vs. *Schizophrenic.*— The depressives had higher mean ratings on the following symptom scales:

Self-blaming behavior*	5
Fluctuations of mood	30
Suicidal tendencies	40
Exaggeration of affect	54

The schizophrenics had higher mean ratings on the following symptom scales:

Overactivity	
Unaware of the feelings of others*	8
Personal neglect*	16
Bizarre or obscure thinking*	24
Feelings of persecution	26
Lack of insight	34
Failure of affect*	41
Relevance of words to recognizable ideas	48
Forgetting of earlier insights	50

They also had higher mean scores on the Wittenborn Clusters:

Depressed state
Schizophrenic excitement*
Paranoid condition*
Paranoid schizophrenia*
Hebephrenic schizophrenia*

4. *Response: Psychoneurotic Recovered* vs. *Not Recovered.*—The Not Recovered had higher mean ratings on the symptom scales:

Pessimism	22
Feelings of anxiety	28
Lack of insight	34

They also had a higher mean score on the Minnesota Psychasthenic Scale.

5. *Response: Psychoneurotic Improved* vs. *Not Improved.*—The Improved had a higher mean rating on the symptom scale.

Lack of Insight (34).

The Not Improved had a higher mean rating on the symptom scale.

Social Withdrawal (13).

They also had a higher mean score on the Wesman Verbal Reasoning Test.

6. *Response: Depressive Recovered* vs. *Not Recovered.*—The Recovered had a higher mean rating on the symptom scale.

Self-Blaming Behavior (5).

The Not Recovered had a higher mean rating on the symptom scale.

Demands for Attention* (31).

7. *Response: Schizophrenic Improved* vs. *Not Improved.*—The Improved had a higher mean score on the Minnesota Scale.

The Not Improved had higher mean ratings on the following symptom scales:

Unaware of the feelings of others	8
Social withdrawal*	81
Difficulty in carrying out plans	21
Pessimism	22
Slowing of response	32
Impaired judgment of likelihood	44
Efficiency impaired by anxiety	49
Forgetting of earlier insights	50
Exaggeration of affect	54
Lack of cooperativeness	55

They also had higher mean scores on the Wittenborn Clusters:

Depressed state*
Hebephrenic schizophrenia*

In addition, they had a higher mean score on the Minnesota Schizophrenic Scale.

Overlap of Symptoms

The assessments of symptoms on the Wittenborn Scales confirmed very clearly the enormous extent to which symptoms overlap from one psychiatric diagnosis to another, even when the assessment of symptoms and the decision as to diagnosis are made by the same physician. If psychiatric diagnoses described well-segregated classes similar to "good" biological species or the diagnoses of general medicine, certain symptoms or

combinations of symptoms would occur in all members of a class and be absent from the members of all other classes, or the position would approximate this. Actually, the situation is far otherwise, as Table 1 illustrates. This lists the

TABLE 1.—*Symptoms Present in at Least 60% of any Diagnostic Class*

Wittenborn Scale	Symptom	Psychoneurotics	Depressives	Schizophrenics
1	Sleeping difficulties	87%	79%	76%
2	Rapid change of ideas	61%	68%	37%
6	Lack of self-assertiveness	61%	37%	43%
12	Irritability	70%	53%	57%
13	Social withdrawal	57%	53%	70%
22	Pessimism	65%	84%	68%
24	Bizarre or obscure thinking	9%	11%	76%
28	Feelings of anxiety	91%	74%	57%
34	Lack of insight	57%	53%	72%
41	Failure of affect	13%	11%	74%
43	Indecisiveness	57%	63%	59%
49	Efficiency impaired by anxiety	70%	58%	45%
Total number of cases		23	19	51

symptoms, 12 in number, which were present in at least three-fifths of any diagnostic class and shows the proportion of each class exhibiting them. For purposes of easy comparison, the figures have been converted into percentages. It will be observed that not one of these symptoms is completely absent from the other classes and only two (bizarre, or obscure, thinking and failure of affect) occur in fewer than 20% of the other classes.

These last two are present in about three-quarters of the schizophrenics and are the most definitely segregating symptoms. How unsatisfactory they are is displayed by Table 2. If the presence of both bizarre thinking and failure of affect is taken as definitive of schizophrenia, then 40% of the patients here diagnosed as schizophrenic would be excluded and 5% of those diagnosed as depressive included. If the presence of one or other or both is taken as definitive, then 10% of patients here diagnosed as schizophrenic are still excluded, while 22% of the psychoneurotics and 16% of the depressives are included. More complex combinations of symptoms lead to no more definitive a segregation.

TABLE 2.—*Distribution of Bizarre Thinking and Failure of Affect*

Symptoms	Psychoneurotics	Depressives	Schizophrenics
Both bizarre thinking and failure of affect	0%	5.3%	60%
Bizarre thinking only	9%	5.3%	16%
Failure of affect only	13%	5.3%	14%
Neither bizarre thinking nor failure of affect	78%	84%	10%

The overlap of symptoms is almost certainly the principal reason for the well-known "unreliability" of psychiatric diagnoses, i.e., the circumstance that equally experienced psychiatrists in diagnosing the same set of patients tend to disagree on something in from a third to a half or more of the cases. The facts noted in this section are strong arguments in favor of a dimensional and profile approach to the problems of psychiatric diagnosis along the lines developed by Wittenborn.

Relationships Within and Between Assessments

The tests of abilities, the Wittenborn weighted cluster scores, and the Minnesota raw scores were intercorrelated for the complete sample of 100 cases (product-moment formula). The results, which will be of interest to other workers with the Wittenborn and the Minnesota Scales are set out in Table 3. The Minnesota M/F scores were correlated separately for male and female patients.

The following points about these intercorrelations appear noteworthy.

A. *Tests of Abilities.*—1. Out of the 51 correlations of tests of abilities with symptomatology, 41 are negative, though only 6 of these are statistically significant. This negative relationship would appear to be meaningful.

2. Two of the three tests had a statistically significant correlation with the Minnesota Question Score.

B. *Wittenborn Weighted Cluster Scores.*—(1) The scores are not completely independent but show a definite oblique relationship.

(2) The clusters Schizophrenic Excitement and Hebephrenic Schizophrenia seem virtually indistinguishable in this population.

3. Depressed State is undoubtedly a misnomer, in view of its correlations about the value of 0.5 with the schizophrenic factors and the circumstance, already noted, that it was higher to a statistically significant degree in the patients diagnosed as schizophrenic than in those diagnosed as depressive.

C. *Minnesota Raw Scores.*—1. The scales show a considerable degree of interdependence. The existence of several of them as genuinely separate factors seems rather doubtful, at any rate in this population. The Schizophrenic and Hypomanic scores have an especially high relationship.

2. The Paranoia Scale is relatively independent of the others.

3. The correlations correspond fairly closely to those obtained by Wheeler, Little, and Lehner [4] with a male neuropsychiatric sample of 110 cases, except that the Paranoia Scale is more independent than in that sample and the Hypomanic Scale more closely related to the others, especially the Schizophrenic Scale.

D. *Relationship of Wittenborn and Minnesota Scores.*—1. The intercorrelations are for the most part low. Quite a few are statistically significant, but not many are even moderately high. In general it might be said that there is very little relationship and no real correspondence of diagnostic terms.

2. The only correlations showing any substantial relationship are the Wittenborn Depressed State score and the Minnesota Depression Scale and the Wittenborn Hebephrenic Schizophrenia and Phobic-Compulsive scores with the Minnesota Paranoia Scale.

3. The relationship between the Wittenborn and Minnesota assessments of schizophrenia is rather slight.

Criticism of the Wittenborn Scales

The Wittenborn system is probably the most adequate answer yet afforded to the research worker faced with the problem of psychiatric diagnosis. It gives explicit recognition to the dimensional character of psychiatric symptoms and their overlap from one diagnostic class to another. Besides giving them quantitative expression, it reduces their relationship to manageable proportions. The care taken in constructing and cross-validating the system is probably unparalleled in the field concerned. Nevertheless, it cannot be considered as the final solution or as beyond amendment and improvement. Ultimately, clusters arrived at by factor analysis can be regarded only as provisional classifications until their regular occurrence has been demonstrated in a number of samples by diverse workers and until, if possible, their observable correlates have been identified. More immediately, difficulties arise in assessment from the verbal formulation of certain scales and from the fact that some scales imply theoretical viewpoints not shared by all psychiatrists.

Throughout the present investigation various murmurings of distaste for different aspects of the scales were heard from the psychiatric raters concerned. To secure more precise information on the matter, these psychiatrists (six in number) were asked some time after the conclusion of the inquiry, when they had rated substantially more patients, including those of other types, to answer a questionnaire indicating whether they (1) found an atomistic, analytical approach of this sort irritating; (2) would prefer a constantly defined scale for all

symptoms rather than separately defined levels for each one; (3) found any scales or levels particularly objectionable, and, if so, why; (4) considered that any symptoms had been omitted which should have been included.

Four stated that they did not find any atomistic approach irritating; two stated that they did, but one of these regarded it as a necessary evil. Three would have preferred constantly defined levels, and three would not (one for an erroneous reason).

There was almost unanimous objection to Scales 9, 25, 29, and 42 because they inextricably confused the possibilities of psychological reactions to genuine physical disease with hysterical behaviors. Scale 29, moreover, implied an hypothesis of the emotional causation of physical disease which most of these psychiatrists considered open to question. Rather similarily, Scale 46 confused organic memory defects with hysterical defects of memory. Scale 34, lack of insight, was found difficult to apply to psychotics and appeared to involve several dimensions, e.g., understanding of others, concealment, and present adjustment. Scale 24 did not allow of distinguishing bizarre thinking disorders from rational delusions. Scale 40 did not permit a distinction between genuine and histrionic suicidal attempts. The differentiation of levels was found insufficiently clear in Scales 6, 17, 23, 27, and 51. The distinction between Scales 19 and 35 was not explicit enough.

The consensus was that the utility of the scales would not be enhanced by the inclusion of further symptoms, since views on this matter would vary according to the training and theoretical outlook of the psychiatrist. Among symptoms noted as not adequately covered, however, the following were most prominent: bewilderment and puzzlement; depersonalization and derealization; degree of talkativeness; repetitiveness in speech; impairment of orientation; degrees of confusion; appropriateness of behavior to chronological age, and abnormal feeding habits (gluttony, picas, etc.).

In general, difficulty was found in applying the scales to organic patients. It was thought that the time reference of the scales as a whole should be very precisely delimited, owing to the problem presented by fluctuation of symptoms or sudden changes in behavior, e.g., the patient who is strongly suicidal up to an attempt but who, after that has failed, becomes entirely unsuicidal.

Comment

The findings that demand most emphasis are those relating to therapeutic response. If these symptomatic differences between patients that do well and the remainder can be confirmed in another sample, it should be possible to go on with an attempt to find their biological (and perhaps sociological) correlates; thereby basic knowledge in the field can be advanced. It should also be possible to use the suggestions of these symptomatic differences toward the development of ways by which the therapeutic response of the prognostically unfavorable can be improved.

The diagnostic differences in symptoms are less important, for the reasons already noted. Attention should, however, be drawn to the striking evidence of the extent to which symptoms overlap among diagnostic classes.

The Wittenborn system of quantified multiple psychiatric diagnosis is evidently capable of some improvement. The same applies to the Minnesota Scales. It seems a pity that these techniques of assessment, which have such great merits, should become fossilized into an unchanging form. A difficulty about the Minnesota System, which has not yet been mentioned here and which is rarely referred to in the literature, is that presented to persons of average or

lower general intelligence by the questions containing a negative. Frequently they answer these as "False" when what they mean to convey is "True." An instance is A.34: "My face has never been paralysed."

This circumstance appears to introduce a definite distorting factor into the results. A more general criticism of both the Wittenborn clusters and the Minnesota scales is that their denotation by the terms of psychiatric diagnosis is misleading and an unfortunate choice; neutral descriptive terms or noncommital letters would be much preferable.

Our final conclusion would be that further studies of the details of psychiatric symptomatology in relation to the outcome of treatment seem likely to be rewarding.

Summary

The relationship of psychiatric symptoms to diagnosis and the outcome of treatment is investigated by means of the Wittenborn Scales and the Minnesota Multiphasic Personality Inventory.

The subjects are the first 100 informal patients admitted to Fairdene Hospital from April 1, 1953, of whom 51 are diagnosed as schizophrenic, 19 as depressive, 23 as psychoneurotic and 7 otherwise.

While there are quite a few statistically significant differences among the diagnostic categories, there is also a very striking overlap of symptoms among them; it is argued that this emphasizes the need for a dimensional and profile approach to the problems of psychiatric diagnosis.

A smaller number of statistically significant differences is found in regard to the outcome of treatment, but it is argued that, if these are confirmed elsewhere, they are likely to be of greater theoretical and practical importance than the diagnostic differences.

Intercorrelations are calculated among the Wittenborn Cluster scores and the Minnesota Scale scores. Within each approach there is a marked interdependence among the variables, but between the two approaches there is little relationship and no real correspondence of diagnostic terms.

Psychiatric criticism of the Wittenborn Scales is detailed. It is remarked that both these and the Minnesota Scales seem capable of considerable improvement.

The senior medical staff of the Fairdene Hospital assisted in rating the patients on the Wittenborn Scales. Mrs. J. P. A. Gillies, psychological technician, applied the psychological tests and assisted in the statistical computations.

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TABLE 3.—*Intercorrelations*

Variable No.	Name	No. of Variable 2	3	4	5	6	7	8	9	10	11	12
1	Wechsler Vocabulary	564	523	−018	071	061	−210	−241	−107	−188	−160	−121
	Wesman											
2	Verbal Reasoning	2	552	−067	−113	−037	−206	−268	−107	−172	−224	−074
3	Numerical Reasoning		3	046	−008	−031	−121	−183	002	−154	−118	−089
	Wittenborn											
4	Acute anxiety			4	209	186	293	131	285	075	043	701
5	Conversion hysteria				5	328	−094	052	−093	−130	−008	271
6	Manic state					6	−148	418	332	054	355	157
7	Depressed state						7	552	249	531	515	160
8	Schizophrenic excitement							8	551	728	861	060
9	Paranoid condition								9	709	423	033
10	Paranoid schizophrenia									10	613	002
11	Hebephrenic schizophrenia										11	000
12	Phobic-compulsive											12
	Minnesota											
13	Question											
14	Lie											
15	K											
16	Validity											
17	Hypochondriasis											
18	Depression											
19	Hysteria											
20	Psychopathic deviate											
21	Interest (Males: N=40)											
22	Interest (Females: N=60)											
23	Paranoia											
24	Psychasthenia											
25	Schizophrenia											
26	Hypomania											
	(Reported separately)											
27	Total stresses											

Significance of Correlations

In general N=100
Significant at 5% level.....r=0.197
Significant at 1% level.....r=0.256

of Assessments, Etc.

13	14	15	16	17	18	19	20	21	22	23	24	25	26	27
198	−102	051	−159	−141	−109	056	−019	−091	−195	−066	−064	−155	−162	127
186	−136	033	−064	−105	−023	043	192	079	−057	−092	051	−027	028	237
340	−117	086	002	−162	−026	−001	160	−171	−265	−217	−029	−055	−026	217
074	−032	−112	043	017	296	244	114	−123	−177	290	098	280	164	048
−018	078	084	138	200	198	101	134	−037	161	097	124	130	−011	025
−013	−024	036	021	−033	−035	030	046	−170	145	183	076	245	−026	313
087	067	026	151	225	338	245	160	−105	156	286	282	231	277	−009
090	115	192	060	091	093	196	035	−268	040	211	091	069	360	204
082	−083	044	121	019	−022	−019	−062	167	150	200	071	039	087	111
036	038	123	077	076	030	126	−003	−138	048	190	122	020	086	023
069	073	109	176	199	044	279	054	−147	093	303	200	180	181	225
015	−076	−137	022	129	196	077	083	056	−103	339	101	245	193	097
13	−046	008	−154	−152	−151	098	016	−298	−032	−064	−055	−110	−089	179
	14	502	−344	−147	−056	019	−282	−203	−314	048	−100	−339	−447	−376
		15	−524	−338	023	147	−331	−381	−315	−245	−293	−538	−575	−327
			16	553	465	100	690	485	581	069	633	721	845	377
				17	586	505	307	073	178	093	278	562	504	226
					18	671	553	046	151	435	519	704	630	285
						19	−067	−204	209	359	359	404	342	300
							20	503	556	100	638	616	778	508
								21	...	045	391	516	560	018
									22	076	464	450	570	259
										23	145	297	198	188
											24	619	738	376
												25	844	536
													26	468
														27

Where N=60
Significant at 5% level.....r=0.255
Significant at 1% level.....r=0.331

Where N=40
Significant at 5% level.....r=0.312
Significant at 1% level.....r=0.403

Relation of Amobarbital Test to Clinical Improvement in Electroshock

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While many theories about the mode of action of electroshock therapy have been offered, the relationship among neurophysiological and psychological factors remains poorly understood.* Although changes in brain function may be demonstrated on electrical recording, such evidence of impaired function has not been correlated with the degree of psychiatric improvement. Similarly, although memory defects and impaired learning ability are common manifestations following the administration of electrically induced convulsions, their severity is not an index of therapeutic outcome. It would appear that the results of ordinary clinical and laboratory procedures and psychological tests do not furnish adequate criteria for a correlation of the alterations of behavior with the changes in brain function.

In previous studies [3] it has been suggested that the therapeutic action of electroshock therapy was related to the production of a milieu of brain dysfunction in which denial of illness (anosognosia) might occur. A concept of anosognosia was advanced which included not only denial of hemiplegia and blindness but denial of many other aspects of illness and problems of living. It was indicated that anosognosia was not explicable as a focal deficit but was, rather, a manifestation of a reorganization of perceptual symbolic function in which the patient represented his problems in an altered language pattern. In the verbal sphere these language patterns included explicit denial, disorientation for place and time, reduplication (reduplicative paramnesia), paraphasia, and confabulation. The patient's feelings about his illness and incapacities could also be manifested in nonverbal aspects of behavior, such as selective withdrawal, inattention, and muteness (akinetic mutism), altered sexual behavior, and euphoric, manic states. The particular form of symbolic adaptation that was used was closely related to features of the premorbid personality.

These changes in behavior were found commonly with infiltrating neoplasms, with acute vascular lesions, particularly when associated with subarachnoid bleeding, and following lacerating brain injury. The electroencephalographic records showed diffuse slow-wave rhythms, and it appeared that the lesions affected the diffuse projection systems rather than any specific discrete projection area. Similar forms of behavior may appear after the operation of prefrontal lobotomy and, in more transitory form, after the administration of electroshock convulsions. When the degree of brain damage was insufficient to permit the elicitation of explicit denial and disorientation on ordinary clinical examination, these phenomena might be observed when the patient was interviewed after the intravenous administration of amobarbital (Amytal) sodium. This

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* References 1-2.

observation furnished the basis for the "Amytal test" for brain damage, in which the persistence of certain patterns of denial and disorientation are considered as evidence of impaired function.†

It was reported that in some patients receiving electroshock treatment for intractable pain, the amobarbital test, which was previously negative, became positive after a number of convulsions. Others received as many as 18 shocks without change in the results of the amobarbital test. It was noted that in patients who gained relief from their complaints of pain, the amobarbital tests became positive, whereas in those patients who continued to complain of pain the amobarbital tests remained negative. The purpose of the present paper is to determine the relationship between the clinical response to electroshock treatment and the results of the amobarbital test in patients hospitalized for psychiatric illness.

Method

Each patient was given a series of amobarbital tests. In this test, the patient is asked a standard group of questions pertaining to orientation and the awareness of illness. The drug is then administered intravenously in a 0.5% solution at a rate of 0.05 gm. (1 cc.) per minute until nystagmus, slurred speech, drowsiness, and errors in counting backward are noted. The same questions are then repeated. The following changes, when persistent, are called "positive" and are deemed indicative of cerebral dysfunction.

1. Complete denial of illness
2. Denial of major aspects of illness, such as attributing entry into hospital to a trivial or past illness
3. Misnaming the hospital, either its proper name or in terms of some euphemism, such as "rest home"
4. Displacement of the location of the hospital. such as to another city
5. Confabulated journey
6. Reduplication of the hospital, such as the patient's stating that he is in another hospital of the same or similar name
7. Disorientation for time of day with confusion of day and night
8. Gross misidentification of the examiner, such as calling him a "lawyer" or an "entertainer"
9. Disorientation for year

† References 4-7.

The patient was given his first test prior to treatment and was retested at weekly intervals. All patients in the series had negative amobarbital tests prior to the initiation of therapy. Treatments were administered three times a week, so that the patients were generally tested after every third treatment. A test was given two days after a treatment and was continued at weekly intervals after the termination of therapy until the result had become negative.

Electroencephalographic records and standard tests of memory and learning ability were also given, but will not be considered in detail in this paper.

Population

Twenty-four patients at Hillside Hospital receiving electroshock with the Reiter Electrostimulator were studied. The patients were not selected by us but were taken on the basis of consecutive referrals by the clinical staff. Some patients were necessarily excluded because their treatment was terminated or interrupted before they were adequately studied. Another patient was omitted because he had manifestations of brain disease and a positive amobarbital test prior to electroconvulsive therapy. The number of treatments varied from 9 to 33. Patients who showed clinical improvement tended to receive fewer treatments. Some of this variability could also be ascribed to differences in the inclination of the resident psychiatrists to use this form of treatment. One patient decided for himself that he had had enough treatment and eloped. Diagnostically, the patients consisted of 14 with depressive reactions, 9 with schizophrenia, and 1 with a manic reaction. There were 15 women and 9 men, and the ages ranged from 24 to 68, with a median of 47 years.

Evaluation of Response to Electroshock Therapy.—All patients were observed for at least eight weeks after completion of treatment. Determination of the patient's response to electroshock was made on the basis of the resident psychiatrist's impression, staff opinion, the nurses' notes, and the clinical evaluation of one of us (M. F.), who supervised the treatments but was not aware of the amobarbital test results. On this basis the patients were divided into three groups.

A. Markedly Improved: The 11 cases in this group were regarded as showing recovery or marked improvement. These patients no longer showed the symptoms which brought them into the hospital; their doctors felt they were better, and the nurses noted them as being able to sleep without medication, eating better, getting along with the other patients, and participating in hospital activities.

B. Moderately Improved: The six patients in this group showed some improvement but con-

tinued to manifest indications of mental illness. These patients typically showed symptomatic relief; i.e., acute depressive features might be gone, but the dramatic change, so evident in the first group, was not apparent. Each patient continued to show some noticeable disturbance, such as obsessional thinking, paranoid ideas, or somatic preoccupation.

C. Minimally Improved or Unimproved: In this group was placed seven patients in whom change was not clearly noticeable or who showed only equivocal or transient improvement. Some showed fluctuations in behavior, at times appearing somewhat improved. But the change was not sustained, so that by the end of treatment they appeared much as they did before.

We are aware of the difficulties in evaluating improvement. Others may have differed in the estimates of changes in these patients. In any case, by using this threefold classification, the differences between the first and the third group will be distinct.

Observations

A. Distribution of Positive Reactions.—The number of amobarbital tests given to each patient during the course of electroshock ranged from 3 to 13, depending on how long treatment was maintained. In Table 1 the data are shown for the number of tests given during treatment and the number and percentage positive for all the patients in each group. The markedly improved patients showed many more positive reactions than the unimproved group, with the moderately improved patients between these groups. Every markedly improved patient had at least one positive amobarbital reaction during treatment. On the other hand, one of the moderately improved patients and five of the unimproved patients never showed a positive result. A comparison of the results in each group, using the χ^2 test, is statistically significant at better than the 1% level of confidence.

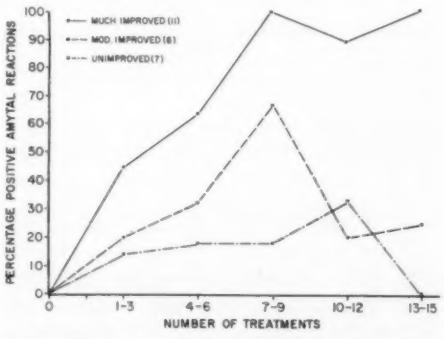
B. Positive Reactions at Each Stage of Treatment.—In the Figure the groups are compared for the percentage of patients in each group who had positive results at each stage of treatment.

Almost half the markedly improved patients had positive reactions after only three

TABLE 1.—*Distribution of Positive Amobarbital Tests During Treatment*

	No. of Tests Given During Treatment	No. Positive	% Positive
Markedly improved (11)...	50	38	76
Moderately improved (6)..	39	15	38
Unimproved (7).....	45	6	13

treatments, and all had positive reactions after seven to nine treatments. In the unimproved cases, on the other hand, the number of positive reactions was small and there was no consistent increase during the course of treatment. Again, the moderately improved group tends to fall between the other two.



Percentage of positive amobarbital test reactions occurring in each group at different stages of treatment.

Although some patients received more than 15 treatments, the data are not presented beyond this point because the number in each group became too small for purposes of comparison. Four of the unimproved patients received more than 20 treatments, with consistently negative amobarbital test results. One of the moderately improved patients received over 30 treatments, with only an occasionally positive reaction.

C. Duration of Positive Reactions.—There were variations in the persistence of positive reactions from week to week. With at least two consecutive positives as the criterion of persistence, nine of the markedly improved, two of the moderately improved, and only one of the unimproved group showed persistent positives. After

the termination of treatment all patients but one had negative amobarbital reactions nine days after the last convulsion. The remaining patient developed a negative test during the second week after treatment.

D. Factor of Age.—Since the patients in the markedly improved group tended to be older persons suffering from depressive reactions, it is conceivable that the difference in amobarbital test results may be related solely to age and only coincidentally to clinical improvement. Underlying this is the assumption that the older person is more likely to show signs of altered brain function when given electroshock. In Table 2 the mean age for each group is shown.

TABLE 2.—*Relationship of Clinical Improvemen To Age*

	Mean Age, Yr.
Markedly improved (11)	47.64
Moderately improved (6)	50.00
Unimproved (7)	35.29

It is apparent that the first two groups were older than the unimproved patients. Yet, while the mean age of the moderately improved patients is slightly higher than that of the markedly improved group, these patients still had significantly fewer positive reactions.

In Table 3 the number of positive reactions during treatment is shown for each group when the analysis is limited to patients more than 40 years of age. In this Table the relationship of positive reactions in the different groups remains unchanged from that when the groups are considered as a whole.

Other Aspects of Behavior

Apart from explicit denial of illness and disorientation, there were changes in behavior that occurred both under the influence of the drug and clinically during the course of treatment in significantly progressive fashion in those patients who improved. These aspects may be divided into verbal and nonverbal communication.

A. Changes in Verbal Language.—These changes consisted of denial expressed in evasion, in negative expressions, and in the use of a syntactical pattern involving the third and second persons. When asked about their symptoms, patients gave such answers as "It's hard to say," or "I forgot," or "I don't know; I've been waiting for the doctors to tell me." The change in syntactical pattern is illustrated by such remarks

TABLE 3.—*Distribution of Positive Amobarbital Tests in Patients More Than 40 Years of Age*

	No. of Tests Given During Treatment	No. Positive	% Positive
Markedly improved (10)	46	35	76
Moderately improved (5)	34	15	45
Unimproved (3)	17	0	0

as "It's what *they* call a depression," or "I'm afraid *somebody* will get hurt," or answering the question "What is your main trouble?" with "What is *your* main trouble?" Sometimes patients would talk of a relative who was sick.

In patients who improved there was a notable development of such patterns in a nondrug interview. One such patient, for example, when asked prior to the start of treatment what his main trouble was, said, "I'm depressed." After two treatments he answered the question with "I don't get along well with my mother-in-law." After five treatments he said, "I don't get what you mean"; after eight, "I get sick; that's all I know." After 10 treatments he said, "Right now, it's that I don't see my wife," and after 11 treatments he said, "In what way do you mean?" and "I don't know how to explain it." At the termination of treatment, his main trouble was given as "I want to get home," followed by an account of how "good" his wife was.

In the unimproved group, on the other hand, the increased use of these language patterns did not occur. They were not present in some and were minimally or inconsistently noted in others. In some of the unimproved patients there were actually fewer such language patterns under the

effects of the drug than there had been in the preamobarbital interview.

B. *Changes in Nonverbal Behavior.*—Euphoric reactions occurred in both clinical and drug interviews most frequently in the markedly improved group, less often in the moderately improved group, and least often in the group which were considered unimproved. In the unimproved patient classed as manic, euphoric behavior was present in his clinical behavior and was not changed by amobarbital.

Changes in sexual behavior appeared during the amobarbital interviews of four of the markedly improved patients but in only one patient in each of the other categories. This took the form of trying to hug or caress the examiner, making remarks with sexual content, or engaging in masturbatory activity. A patient in the unimproved group showed this behavior both during pre-drug interviews and under the influence of amobarbital.

Withdrawal or "selective inattention" was shown by 9 of the 11 markedly improved patients, particularly during the drug phase of the amobarbital interview. This behavior consisted of failure to answer the questions about illness and hospitalization or responding in dysarthric and cryptic fashion. This reaction under the drug occurred only once in each of the other groups. It was of interest that two patients in the unimproved category who appeared withdrawn before the test became more responsive under the influence of the drug.

Comment

The results of the amobarbital tests in these patients indicate that there is a relation between clinical improvement and the production of brain damage or an altered state of brain function as determined by this particular method of examination. In patients who improve, the amobarbital test becomes consistently positive early in the course of treatment. In moderately improved or unimproved patients there are fewer positive reactions and their frequency does not increase with more treatments. With other methods of evaluating brain function such close correlation was not present, as all patients showed abnormalities in the electroencephalographic record and impaired learning was found as frequently in patients who improved as in those who do not. The significance of this relationship may be more clearly appreciated by a consideration of the changes in symbolic function that occur in states of altered brain function.

It has been useful in studying the behavior of patients with alterations in brain function to distinguish between defects in the formation of symbol patterns and changes of language patterns which indicate a shift in the mode of interaction in the environment. In the first category may be included many types of memory defects, dyscalculia, topographical disorientation, and aphasia. A patient with such a memory defect cannot select elements of experience, classify them into significant units, and arrange them into a temporal pattern. These defects are observed with diffuse cortical lesions and probably occur universally after shock treatments in transient fashion. They are, however, related very remotely, if at all, to therapeutic outcome. Alterations in the mode of interaction in the environment are exemplified in the various patterns of disorientation and denial and in the amnesias that are noted with lesions of the diffuse projection systems, in chronic barbiturate intoxication, and following electroshock convulsions. Here there is no defect in memory, awareness, or perception as such, but the patient selects or rejects certain aspects of the environment for the expression of his own motivations. In disorientation for place, for example, the misnaming and mislocating of the

hospital serve as symbolic representations of the patient's feelings about his incapabilities and problems—often as the manifestation of his need to be well and go home. It is not that the patient is unaware of his problems and does not know where he is in an absolute sense. He commonly "remembers" the name of the hospital and expresses "awareness" of his difficulties in other contexts of language. The unawareness is, rather, of the far greater degree to which he is expressing his own motivations in his perception of the temporal, spatial, personal, and somatic aspects of the environment.

In considering what constitutes therapeutic improvement, it is evident that the evaluation that is commonly made by a hospital staff depends in large part on the particular types of symbolic adaptation and defensive operations that are used. If the patient denies that he has any problems or that he is troubled by them, or if he cannot recall any, he is rated as improved. Such patients characteristically appear affable and uncomplaining, their manner reinforced by clichés and banalities, themselves adaptive forms of language. Many studies ‡ have shown that general memory impairment does not persist after electroshock but that there is a selective "forgetting" of traumatic material in the patient's life. This does not mean that he has developed a better understanding of his interpersonal relationships or has acquired "insight." The observation is also significant in explaining why, although electroshock may have a short-term beneficial effect, evaluation of long-term results shows little difference between treated and untreated cases. Also, the fact that therapeutic improvement did not result in patients with negative amobarbital tests suggests that methods of administering electroshock by minimally affecting brain function, such as a unilateral seizure, will not prove generally efficacious. From the immediately practical standpoint, the amobarbital test given after the third or fourth treatment may be of prognostic value.

The amobarbital test is not in itself a direct index of brain damage in that it measures some particular modality of dysfunction or brings out a specific defect. Rather, under the conditions in which it is given, one deduces impaired neural function by reason of the change in the organization or pattern of language in which the patient expresses himself. A positive result requires not only that a certain degree and type of impairment of brain function exist but that the patient employ verbal denial and disorientation as adaptive mechanisms. It would be expected that among patients with equivalent degrees of brain damage the highest incidence of positive amobarbital tests would occur among those who characteristically use denial as an adaptive mechanism in stress.

In relating these findings to the mode of action of electroshock and other somatic therapies, several considerations seem of importance. There is a combination of an added stress and a change in brain function. The milieu of brain function determines the pattern or organization of the adaptive behavior which can be most clearly formulated in terms of language. These include not only verbal patterns of denial and disorientation, elicited with the aid of the drug, but changes in syntactical patterns indicative of an altered relationship of the self in the environment. There were also indications that in the improved patients there were more changes in all types of symbolic adaptation, nonverbal as well as verbal. Thus, a patient who appeared withdrawn both in the predrug and in the drug interview had a poorer prognosis than the patient who became withdrawn only under the effects of the drug. The patient who showed altered sexual behavior under the effects of the drug had also exhibited this behavior during

‡ References 8-12.

the clinical questioning as well and did not improve with treatment, whereas the four patients manifesting sexual behavior only under effects of the drug did improve. It is likely that the faculty of changing symbolic patterns regardless of content is a factor in therapeutic improvement.

Summary

Twenty-four patients referred consecutively for electroshock treatment were given amobarbital (Amytal) tests before and at regular intervals during and following the course of treatment.

There was a close relationship between the short-term response to treatment and the results of the amobarbital tests. The much improved patients showed early, persistent, and increasingly positive reactions during the course of treatment. Unimproved patients showed no positive reactions, or showed them infrequently and inconsistently. An intermediate group, who showed moderate clinical improvement, showed more positive reactions than the unimproved group but fell far short of the much improved group in the incidence of positive reactions.

Changes in language and nonverbal forms of behavior related to denial were most consistent and pronounced in the improved group, even in interviews not employing drugs.

These observations indicate that clinical improvement in electroshock requires the creation of conditions of altered brain function in which new patterns of symbolic adaptation can be maintained.

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F-L Fergus Falls Lobotomy Scale

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Introduction

The F-L Fergus Falls Lobotomy Scale, based upon eight easily obtained items, is useful in predicting the chances for improvement and for decreasing the number of poor results of lobotomies on long-term public psychiatric hospital patients. Easily used prognostic ratings or predictive scales have not, to our knowledge, been published. The items include length of hospitalization, leaves from the hospital, remissions, response to electroshock treatment, education, occupation, prepsychotic adjustment, and L-M Fergus Falls Behavior Rating Scale * average. All items are listed routinely in any psychiatric facility except the last, which can be determined by any two untrained ward personnel.

Material and Methods

Original Data.—A study for prediction of results of the standard prefrontal lobotomy on long-term public psychiatric hospital patients was started in 1951. Twenty-six items were recorded; three of these were later eliminated because of lack of data or insufficient number of applications to the group under study. The base rate was 63% (i.e., 63% of the patients operated upon subsequently improved). Hospitals having base rates different from this are referred to the article by Meehl and Rosen * for an explanation of how to use the data in this article.

Characteristics of the Selected Population.—Fergus Falls State Hospital is a 2000-bed public psychiatric hospital serving northwestern Minnesota. From May, 1951, through August, 1953, a total of 103 patients received the standard prefrontal lobotomy; all were operated upon by the same surgeon. Staff psychiatrists or visiting psychiatric consultants selected patients from a pool of long-term patients who presented management problems in terms of disturbed behavior. Patients operated on from March, 1952, through May, 1953, were included in the validation of the Scale (minus one who died); patients operated on from May, 1951, through January, 1952, and June, 1953, through August, 1953, were included in cross validation of the Scale (minus three who died); all were evaluated at least one year postoperatively. The mean length of hospitalization of the validation group was 10.7 years; that of the cross-validation group, 10.9 years. The mean age at operation of the validation group was 43.4 years; that of the cross-validation group, 40.1 years. Schizophrenic illnesses comprised 67.4%, and manic-depressive illnesses comprised 16.3%, of the validation group, a total of 83.7%. In the cross-validation group these figures were 80.4%, 5.4%, and 85.8%, respectively.

Validation.—In 43 consecutive cases all 23 variables were recorded prior to the lobotomy. All 43 cases were evaluated at least one year postoperatively in terms of improvement or lack of improvement. The 23 variables were studied to determine whether any discriminated between improved and unimproved patients. Eight items were found to be useful, some in two directions (positively or negatively), resulting in a 13-point scale, ranging from +8 to −4.

Cross Validation.—The 13-point scale was then applied to patients preceding and following those on whom the scale was validated. These 56 patients were consecutive cases except for the intervening period. Cross-validation results were the same as those on validation. (Reliability: Two other psychologists were asked to rate the present status and position on the F-L Scale, with 82% and 93% interrater agreement, respectively.)

Criteria of Improvement.—"What is the nature of improvement following psychosurgery? It is recognized that in a certain undetermined proportion of improvements or recoveries occurring after psychosurgery, the recovery is unrelated to the psychosurgical process. In the last analysis, the question of whether a patient has or has not been improved must rest upon the decision of whether he now has achieved greater social functioning. Although one conferee accepts lessening of anxiety as evidence of improvement, and another considers psychologic tests useful in arriving at an estimate of improvement, most conference

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* References 1, 2.

members appear to require that lessening of anxiety become manifest in improvement at the social-behavioral level and that changes in performance on psychologic tests are of only incidental interest. Such a person would be expected to show an increase in his range of behavior adaptations. Improvement should be stated in terms of previous behavior, on the basis of clinical examination and ward behavior."[4]

In our study, those patients who were either definitely improved or definitely worse after psychosurgery constituted no problem in classification. For the others, improvement or lack of improvement was evaluated in terms of hospital or nursing management. The following examples are given as a guide:

(*a*) A formerly constantly combative patient who is now combative once a week is not improved; if he is combative only once a month, he is classified as improved.

(*b*) A formerly greatly agitated or aggressive patient who is now withdrawn and incontinent is not improved (or is definitely worse); a formerly agitated or aggressive patient who now sits quietly with no other problems is classified as improved.

(*c*) A patient showing few overt signs of improvement but who now can stay for periods of time with relatives is classified as improved.

Results

Use of Scale—After patients have been selected, this scale can be used to reduce or eliminate the number who will show lack of improvement.

Example A: If final selection for surgery is based on a score of +4 or more

TABLE 1.—*Scoring of F-L Fergus Falls Lobotomy Scale*

F-L Fergus Falls Lobotomy Scale (if rater is uncertain about any item it should *not* be scored)

A. Positive Values: Each of the following is given a score of +1:

1. An average of 3.0 or above on the L-M Fergus Falls Behavior Rating Scale (preferably administered one month preoperatively)

2. Fair or good prepsychotic adjustment (fair is equivalent to "limping along"; for example, working at home with positive adjectival report from relatives and some social activity; see item B 2 below)

3. Skilled occupation for at least six months (successfully owning or operating a farm, stenography, etc.)

4. Specialized education. Any education or training (whether completed or not) beyond high school, or in older patients any education beyond grade school

5. Good response to electroconvulsive treatment whether sustained or unsustained

6. One or more complete remissions

7. Total recorded hospitalization of less than nine years

8. Release from a mental hospital at least once for longer than a month

B. Negative Values: Each of the following is given a score of −1:

1. An average of 1.9 or less on the L-M Fergus Falls Behavior Rating Scale

2. Poor prepsychotic adjustment (negative reports from relatives; for example, "always nervous," "stubborn," "hard to handle"; see item A 2 above)

3. No occupation—patient must never have worked satisfactorily at home or in the community

4. No releases from a mental hospital or releases for less than a month

TABLE 2.—*Results on F-L Fergus Falls Lobotomy Scale*

Scale	Validation				Cross Validation
Score	Improved, Cum %	Unimproved, Cum %	% with Score Shown or Less	Correctly Operated, Cum %	Correctly Operated, Cum %
−4	100	100	100	63	62
−3	100	88	95	66	65
−2	100	81	93	68	71
−1	96	63	84	72	74
0	93	44	74	78	78
+1	81	25	60	85	83
+2	70	25	54	83	82
+3	59	19	44	84	100
+4	48		30	100	100
+5	41		26	100	100
+6	26		16	100	100
+7	11		7	100	
+8	7		5	100	
No. of Patients	27	16	43	43	56

on the F-L Scale, 48% of those who will show improvement will be operated upon; the other 52% who would have shown improvement will be missed, but 100% of those who will be unimproved will be eliminated.

Example B: If final selection is based on having a score of 0 on the F-L Scale, 93% of those who will show improvement will be operated upon; the other 7% will be missed; 56% of those who will not improve will be eliminated.

Comment

This scale was developed and validated on the characteristics of the population available and on the basis of improvement or lack of it as defined in this paper. Collection of data and development of this scale occurred over the four years of this study. Reports of others discuss whether psychosurgery influences discharge rates.†

Of the 23 items studied, 8 were found to be of value in discriminating between those patients who one year postoperatively showed improvement or lack of improvement.

Items showing predictive value included L-M Fergus Falls Behavior Rating Scale, occupation, prepsychotic adjustment, education, response to electroconvulsive treatment, remissions, duration of hospitalization, and releases from hospital.

Items showing no predictive value included sex, marital status, psychiatric diagnosis, type of onset (rapid *vs.* gradual), age at first admission, age at operation, duration of illness, amount of restraint or seclusion, obsessions, compulsions, tension, delusions, mood, suffering, author's predictions.

The items were studied in relation to the population available and may or may not be applicable to other population groups (private practice, clinics, or other types of hospital population). This may be an explanation of differences reported in regard to the predictive value of diagnoses and of symptoms, such as obsessions and compulsions.‡

The factors shown to be of predictive value appear to be related to good personality organization and good prognosis in general. The use of the F-L Scale allows them to be evaluated in a numerically significant manner.

The F-L Scale is of no value in selecting patients for operation; however, when selection has been made, the F-L Scale is of value in predicting results and in eliminating all or a proportion of the patients who can be expected to show lack of improvement.

Conclusions

The F-L Fergus Falls Lobotomy Scale, when applied to long-term public psychiatric hospital patients selected for the standard prefrontal lobotomy, is of value in eliminating from consideration patients whose prognosis for improvement is poor.

Factors and impressions reported by others to be of predictive value were not found by us. Differences in the types of patients operated on may account, at least partially, for these discrepancies.

The factors found to be of predictive value, which may be related to good personality organization and thereby good prognosis in general, have been arranged into a useful numerical scale.

State Hospital, Jamestown, N. D. (Dr. Freeman).

W. L. Patterson, Superintendent of Fergus Falls State Hospital, made this study possible. Adeline Foss, research clerk; Curtis W. Page, psychologist, and Frank P. Amedeo, psychologist, all of Fergus Falls, and Albert Rosen, psychologist, VA Hospital, Fort Snelling, Minn., gave advice and guidance in the study.

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Action of Local Hydrocortisone on Spinal Cord Wounds

Effect on Inflammation, Repair, Degeneration, and Regeneration

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The general systemic effects of adrenocortical steroids is not a primary factor in the delayed healing and diminished inflammatory phenomena of wounds. A primary action of these hormones on the connective tissue elements is now accepted.[1]

The anti-inflammatory action of hydrocortisone may be due to the protection of the mesodermal elements from the injured tissue in the wound.[2] The anti-inflammatory properties have been explained by a direct action on the fibroblast cell,[3] interference with the elaboration of ground substance,[4] and, mainly, alteration in the permeability of the vessels.* The effects on inflammation and repair of local application of hydrocortisone acetate to wounds of the brain and to other parts of the body are similar. The cerebral cicatrix is diminished and proliferation of connective tissue is depressed, as compared with a contralateral wound, at corresponding periods of time, in the same animal.[6]

The action of local hydrocortisone in spinal cord wounds was investigated, and the results are reported in this paper. The study was carried out in partial section of the spinal cord in cats.

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From the Department of Neurology and Neurosurgery, McGill University, and the Montreal Neurological Institute, reprint no. 531.

* References 1 and 5.

Material and Method

Fifty-four young cats were used for this experiment. The animals treated with local application of hydrocortisone acetate were divided into two groups: (1) those with 5 mg. of the powder, and (2) those with 5 mg. of the hormone in suspension.† The suspension was placed in the wound, and a small piece of gelatin sponge embedded in the hydrocortisone suspension was left in contact with the spinal cord wound at closure. For each treated animal there was a control animal.

Laminectomy was performed under pentobarbital (Nembutal) anesthesia. An U-shaped dural flap was turned in the animal with powder application. In the animal with suspension, the laminectomy was longer; and the incision in the dura was 5 cm. in length, and a wide flap was turned. The section of the spinal cord was made with a cataract knife, with the help of a Bromley chordotomy guide, in the high dorsal region. The ventral quadrant of the spinal cord was spared to prevent spinal shock.[7] The dura was left open. When powder was applied, the cord was covered by loose fascia after the dura was turned back into place. The wound was closed in layers.

The animals were on a free diet. Recovery from anesthesia and shock was spontaneous. No antibiotics were given. The animals were killed by exsanguination under pentobarbital anesthesia—at 1½ and 6 hours; 2, 4, 8, 12, 18, 30, 45, and 83 days, and 6½ months. The spinal cord was taken out and placed in 10% formalin. Section of the wound was made longitudinally, and cross sections of the cord were taken 2 cm. above and below the wound. Sections were stained with hematoxylin-phloxine-saffron, Laidlaw's connective tissue stain, cresyl violet, phosphotungstic-acid hematoxylin for

† Hydrocortone Acetate (hydrocortisone acetate) powder and saline suspension of Hydrocortone Acetate were supplied by Merck & Co., Ltd., Montreal.

glia, Weil's stain for myelin, and the Bodian method for axons.

Results

Four animals died, two of infection, one in giving birth, and one of spinal shock. The animals recovered from anesthesia and shock in an average time of 10 hours. There were sphincter disturbances, manifested by retention of urine and feces, in four animals. Leg function returned gradually. The 83-day and the 6½-month animals showed but minimal ataxic movements and slight motor deficit.

The effects of the hormones on (1) the inflammation and process of repair; (2) degeneration, and (3) regeneration are presented. The terminology used is that of Ramón y Cajal,[8] as in Figure 1.

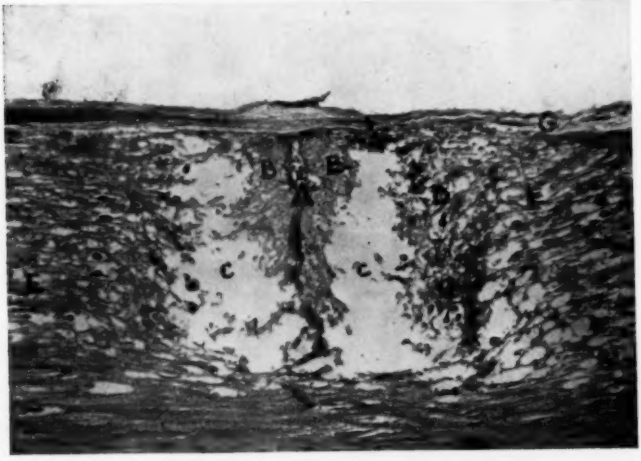

Fig. 1.—Six-hour control wound. *A*, wound tract; *B*, preserved fibers; *C*, necrotic portion of the traumatic degeneration; *D*, degenerated segment; *E*, central and distal stumps; *F*, dura covering the wound. Bodian stain; × 45.

1. *Inflammation and Repair.—(a)* Control: A few hours after the injury (one and one-half and six) the leucocytic infiltration of the white matter was minimal. At two days polymorphonuclear leucocytes were present in great number. In the four-day wound granular cells (Cajal[8]) were present in the necrotic portion. Edema was marked, and plasma exudate was minimal. Fibroblastic proliferation of the pia was light, and neutrophiles in the subarachnoid spaces were numerous. At eight days the granular cells filled the necrotic portion and were present in the white matter itself. Few neutrophiles were present. The vessels extended across the space left by the necrotic segment and showed slight endothelial thickening. Fibroblastic proliferation coming from the pia-arachnoid projected into the wide space left in the wound. At 12 days the space left by the necrotic segment was lined by granular cells and glia, forming a pseudocyst with granular cells within it. There were phagocytes in the degenerated segment. Vessels from the gray matter and fibroblasts from the pia-arachnoid projected into the wound. The acute period of inflammation had stopped, and repair was progressing. At 18 days there were connective tissue, cyst-like cavities, and glia in the depression caused by the autolytic changes in the wound. In the white matter, in the degenerated segment of both stumps, granular cells, and inter- and intratubular (nerve tubes) were abundant. From 18 days on cicatrization depended on the quieting of degeneration with replacement of nerve tubes by granular cells, on the one hand, and, on the other, by the fibroblastic proliferation of the leptomeninges projecting into the scar (Fig. 2). The cyst-like forma-

tion was a constant finding, variable in size and in granular-cell content. This formation caused the invasion of the fibroblasts to be made on the sides and through the vessels.

(*b*) Treated Wounds: There were no differences in the early stages of inflammation as judged by edema and neutrophilic infiltration before the two-day period. The granular cells were diminished in the four-day wound. After 12 days in the necrotic portion the autolytic changes were advanced. There were few granular cells and poor fibroblastic proliferation of the leptomeninges. In the wounds with local application of suspension, the inflammatory phenomena were basically the same: diminished number of granular cells and fibroblastic proliferation, and active necrosis. The vessels were preserved within the degenerated segment. Neutrophiles were numerous in the wounds. There was formation of cyst-like cavities in the depth of the wound.

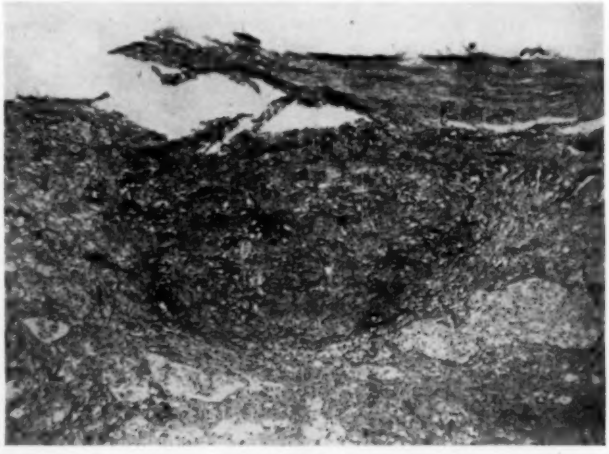

Fig. 2.—Thirty-day control wound. Final scar formed by connective tissue mainly. There is proliferation of connective tissue in dura. Cyst-like formation. Hematoxylin-phloxine-saffron; × 45.

At 16 days there were marked differences between the effect of the powder and that of the suspension. When powder had been applied, the wound could be seen between the preserved fibers; there was poor fibroblastic proliferation in the wound; the autolytic material had disappeared on both sides, leaving an empty space that corresponded to the necrotic portion of the traumatically degenerated segment. When suspension was applied, there was abortive formation of cysts, and there were numerous granular cells in the space left by the necrotic segment.

The suspension-treated wound had healed at 30 days, without formation of cyst-like cavities. The mesodermal scar was diminished. The cavity due to loss of substance was minimal, and the granular cells were abundant (Fig. 3). When powder was applied, healing had not taken place. There was no more necrosis, and there were fibroblasts between the preserved fibers. Between these fibers and the stumps there were spaces with granular cells, vessels, and some nerve fibers that were preserved from degeneration.

At 45 days healing still had not taken place. The space occupied by the preserved fibers revealed a deep-blue-stained material in hematoxylin-phloxine-saffron sections, which resulted from degeneration of the fibers. This was surrounded by a double loop of connective tissue coming from the leptomeninges. To each side there were areolar tissue, connective tissue, and glial cells (Fig. 4).

At 83 days the wound had healed. The connective tissue did not go far into the

Fig. 3.—Thirty-day wound treated with 5 mg. of hydrocortisone acetate in suspension. Diminished scar. No cyst formation. Hematoxylin-phloxine-saffron; × 45.

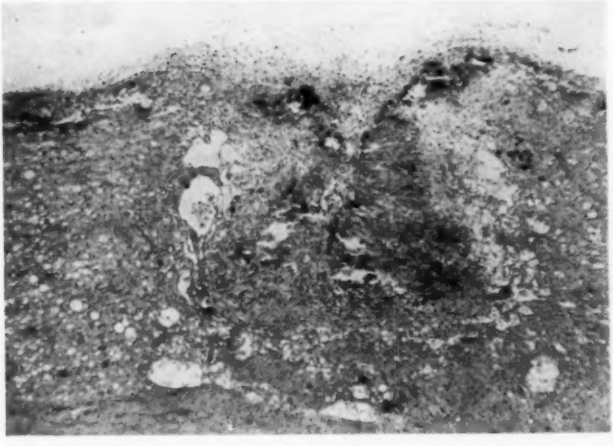

Fig. 4.—Forty-five day wound treated with 5 mg. of hydrocortisone acetate powder. Delayed healing. Different parts of wound can still be identified. Proliferation of connective tissue diminished. Hematoxylin-phloxine-saffron; × 45.

Fig. 5.—Eighty-three-day wound treated with 5 mg. of hydrocortisone acetate powder. Final scar is formed. The connective tissue in scar and proliferation of connective tissue in dura are diminished. Hematoxylin-phloxine-saffron; × 45.

scar; there were cyst-like formations, and retraction was minimal (Fig. 5).

2. *Traumatic and Wallerian Degeneration of Nerves.—(a)* Control: Necrosis caused by trauma took place in one and a half and six hours and was well established in two days, in both thick and fine axons. After eight days the necrotic portion was replaced by cyst-like formations. Changes in the axons and myelin of the nerve tubes in the degenerated segment were marked at five and eight days. Degeneration, judged by the formation of granular spheres at the tip of the axons, granular appearance of the axon, and swelling of the myelin sheath, was nearly complete at 12 days. From then on the traumatic degeneration was mixed with secondary degeneration. Few fine fibers remained between the granular cells in the degenerated stumps. These fibers underwent late degeneration.

Secondary degeneration in the fine axons was observed in the 48-hour specimen and continued up to 45 days.

(b) Treated Wounds: The necrotic segment underwent changes in the early stages. At 48 hours the traumatic degeneration was established in the thick and medium-size axons. Fine axons, interrupted by the section, crossed the necrotic portion in groups, establishing a bridge between the degenerated segment and the preserved fibers (Fig. 6). This bridge was not seen in the 12-day wound, when necrosis had taken place. There was no cyst-like formation.

Degeneration of axons took place up to 16 days, after which there was a gradual change to secondary degeneration. Bead-like formations in axons and swelling of myelin were seen in the degenerated segment, concomitant with swelling and fragmentation of myelin at a distance from the wound. There was degeneration in the medium-size medullated fibers when scar had been formed, at 83 days and 6½ months.

In the early stages there were in the necrotic segment medullated and non-medullated fibers, which reached the margin of the wound as the necrotic segment disappeared. Some of the fibers remained in the space left by the necrosis and were preserved (Fig. 7). There were changes in the tip of the axons throughout the different time periods which were indicative of slow degeneration. In the long-term wounds the number of fibers close to the wound was greater than in the controls and some fibers reached the wound margin. There were also nerve fibers within the connective tissue of the scar itself (Fig. 8).

3. *Regeneration.—(a)* Control: At two and four days there were thickening of axons and some branching of fine non-

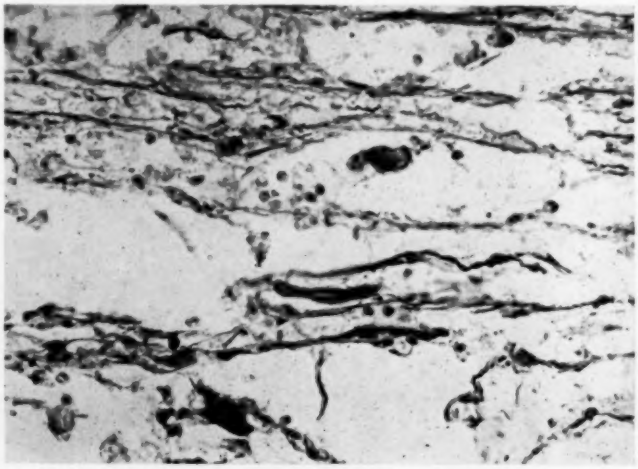

Fig. 6.—Forty-eight-hour wound treated with 5 mg. of hydrocortisone acetate powder. Axons seen in necrotic segment. Bodian stain; × 320.

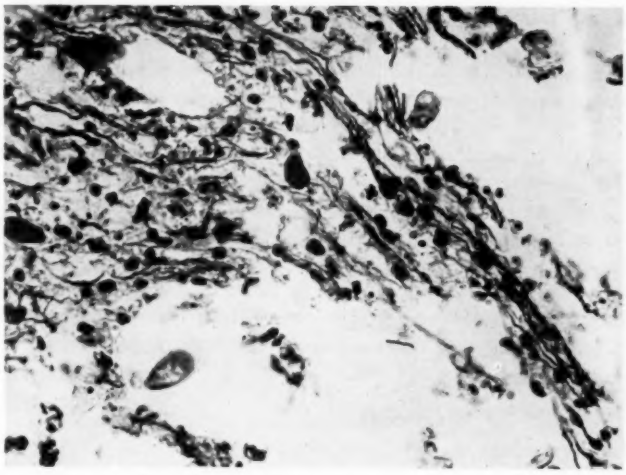

Fig. 7.—Sixteen-day wound treated with 5 mg. of hydrocortisone acetate powder. Axons in necrotic portion bridging between degenerated segment and preserved fibers. Bodian stain; × 320.

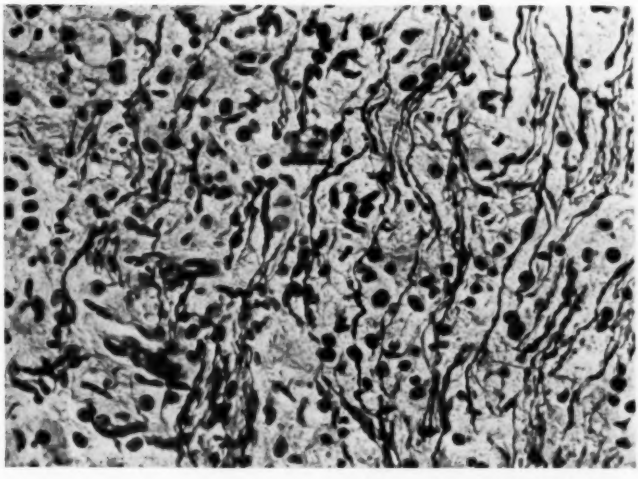

Fig. 8.—Eighty-three-day wound treated with 5 mg. of hydrocortisone acetate powder. Axons present within the scar itself. Bodian stain; × 320.

medullated fibers. The process of branching was intense at 8 days and at 12 days the fibers began to degenerate. At 17 days there was irregular branching of axons, which disappeared in the 30-day wound. A few axons of fine nonmedullated fibers remained in the scar itself. A few fine and medium-size axons were seen in the proximity of the wound. There was no evidence of regenerative phenomena, as judged by thickening or branching of the axons.

(b) Treated Wounds: At two and four days a few fine axons were thickened and showed some branching. In the 12-day wound sprouting of fine axons was seen in the fibers of the necrotic area and in the fibers close to the wound in the degenerated segment. When suspension was applied, there were argentophilia of axons and occasionally branching.

There was no branching of axons in the fibers that reached the wound margin from one month on. Thick axons were close to the wound margin. At one and a half months, medium and small fibers reached the wound margin on both stumps.

At 83 days and 6½ months, when the

scar had been formed, there were abundant nerve fibers in the connective tissue itself, and separated from the vessels. Numerous fibers between the granular cells reached the scar itself. Axons with varicosities, similar to the axons of peripheral nerves, were also present in the cicatrix.

Preserved fibers: Axons were preserved on both sides of the incision for five days. In treated wounds, degeneration began in the 16th day and continued up to 1 month. Fine axons were present up to one month. When the scar was formed, there were fine nerve fibers in it.

Comment

A sharp single partial section of the spinal cord reduced mortality through protection from spinal shock, but did not permit a physiological evaluation of regeneration.

As in the brain, hydrocortisone delayed healing when applied locally in high doses. The early stages of inflammation (edema and neutrophilic infiltration) were not significantly modified. Edema in wounds with powder application was marked; it was considered due to small dural decompression. When the dural decompression was extensive, edema did not occur. The phagocytic activity of the granular cells was depressed and delayed, as judged by the diminished number of cells present in the early stages and the persistence of cells in later stages. The mechanism of this depression may be due to inhibition of the normal stimulus by the hormone. The mechanism responsible for the delayed healing of hydrocortisone in the spinal cord may be the same as in other tissues. The nerve tubes and the nonmyelinated axons play a passive role in the repair of spinal cord wounds.

A zone with preserved fibers on both sides of the wound was a constant finding. The axons were preserved for a longer period of time when hydrocortisone was applied. The mechanism of the preservation of disconnected axons in wounds has not been adequately explained.

Necrosis of myelin and axons is not sufficient to stimulate connective tissue. Hydrocortisone protects the axons, as is indicated by the preservation of the disconnected axons for a longer period of time. The preservation of medium-size and fine axons that survive the acute stages of necrosis and degeneration also suggests the protection of the axons. The prolonged Wallerian degeneration in the cord of treated animals may have the same explanation, that is, protection of the axon at the same level of injury. In peripheral nerves myelin changes in secondary degeneration have been reported unchanged by cortisone.[9]

The question of regeneration of the spinal cord is debated in the literature. Opinions in favor of ‡ and against it § have been advanced. Abortive regeneration, or regeneration inhibited by the mesodermal scar in the spinal cord, has also been mentioned and supported.‖ In the present experiment, the mesodermal scar was diminished in the treated animals. Division of axons, increased affinity of axons for silver, and thickening of the axons (considered signs of regenerating fibers by Cajal [8]) were observed. There was also a greater number of fibers close to the wound and in the final cicatrix itself. The findings suggest that abortive regeneration takes place in the spinal cord. The medium-size and fine axons are protected by hydrocortisone from degeneration. The presence of axons in the immediate vicinity of the wound and in the scar itself may be due to a slow regenerative phenomenon.

Summary

The local action of hydrocortisone was studied by hemisection (with sparing of the ventral quadrant) in the spinal cord in cats.

As in the brain, the inflammatory re-

‡ References 10-17.
§ References 18-20.
‖ References 21-24, 8.

action is diminished. Edema and necrosis of nerve tubes are not altered by the hormone. The healing of the spinal cord wounds is delayed, and the final mesodermal scar is diminished.

Degeneration of thick nerve tubes is unaffected, and medium and fine axons degenerate at a slower rate than controls. Secondary degeneration and myelin changes are delayed but not significantly diminished.

Fine axons are close to the wounds at all periods and within the scar itself in long-term treated wounds, suggesting a protective action of the hormone on the axons.

In the control and treated wounds there are changes in the axons, which are considered evidence of abortive regeneration. These changes are present for a longer period of time in the treated wounds.

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Effect of Reserpine and Open-Ward Privileges on Chronic Schizophrenics

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Reserpine has been described as having a calming or tranquilizing effect on subjects and as exerting its hypotensive and sedative effects through action on the hypothalamus. Plummer [7] stated that probably the most likely region at which reserpine could produce changes in autonomic balance would be "an area of the central nervous system, such as the hypothalamus, where autonomic nervous functions are integrated. . . . All observed effects of reserpine, including sedation, reduced emotional response, peripheral autonomic alterations, and circulatory changes, are explicable on the basis of an alteration of sympathetic-parasympathetic balance by partial suppression of sympathetic predominance at the hypothalamic level." Adler [1] reported in his study that there is a reduction in hyperactivity, assaultiveness, apprehension, anxiety, and depression. Although he noted that patients varied in response to the drug, there was an obvious decrease in anxiety. Similar improvement was noted by Barsa,[2] who selected patients on the basis of their excited, hyperactive, assaultive, or destructive behavior, regardless of diagnosis, age, duration of illness, or previous treatment. Noce * found that the use of the drug reduced considerably the need for electroconvulsive therapy, sedation, restraint, seclusion, and hydrotherapy, and that 30% of paranoid schizophrenics and 45% of catatonic schizophrenics improved markedly. Tyhurst [9] described similar results in his study and suggested that the drug seemed mainly to reduce the emotional disturbance and concern associated with abnormal mental content.

A more recent study, and one with the use of control groups, was carried out by Sommerness and associates,[8] who selected 90 of their most highly disturbed chronic mentally ill male patients and divided them into three groups of 30 each. Thirty were given reserpine (Rau-Sed); 30 were given an identical-appearing placebo, and 30 received no medication. Their conclusions were that reserpine in oral doses of 1 mg. b.i.d. did not effect a behavioral improvement as measured by the L-M Fergus Falls Rating Scale; that it effected a lowering of blood pressure and a slight weight gain, and that the greater attention to the patients inherent in taking blood pressures and weights and increasing the interest of ward personnel resulted in behavioral improvement of all three groups under study.

With the exception of the aforementioned investigation, there appear to be no studies in the literature in which adequate control groups were used in experimenting with the use of reserpine with chronic schizophrenic patients. It has been pointed out by Wolf and Pinsky [10] that patients have shown both psychological and physiological changes when given placebos, and it was felt by us that the effect of the drug must be evaluated with comparable control groups who are to be given placebos or no medication.

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Chief Clinical Psychologist (Dr. Penman); Director of Professional Services (Dr. Dredge), Veterans Administration Hospital.

* References 5 and 6.

It is possible that the changes in patients as a result of receiving placebos are due to suggestion, increased attention, and changes in ward routine.

Hypotheses

In general, the studies of the effect of reserpine have indicated a marked reduction in anxiety, hyperactivity, assaultiveness, depression, apprehension, and concern associated with abnormal mental content, and in some instances remission of all symptoms associated with the patient's illness. We set out to evaluate these reported effects of reserpine in a controlled study and, in addition, to observe the effect of granting open-ward privileges to patients who have been on a locked ward for considerable periods of time. The latter was done with the hope of reducing some of the administrative problems of a closed ward, provide added incentive to the patients, and make more open-ward beds available in the hospital. It was also felt that the use of reserpine would result in some patients' making a good open-ward adjustment, whereas previously they had been unable to do so. With these general statements in mind, we tested the following specific hypotheses:

1. Reserpine has a tranquilizing effect on patients which will result in behavioral improvement beyond that which can be attributed to suggestion, increased attention, or changes in ward routine.

2. Open-ward privileges will motivate the patients to change their behavior in an acceptable direction, and will result in increased socialization.

3. Patients receiving reserpine will conform to open-ward rules and regulations, and make a more adequate adjustment to open-ward privileges than patients receiving placebos or no medication at all.

Experimental Procedure and Population

Since the experiment was designed to measure two variables, the effect of placing the patients on open-ward status and the effect of reserpine, it was necessary to select the group from one ward and to include patients who were not known elopers. The Chief of Professional Services and the ward physician of one of the Continued Treatment Service wards interviewed all of the 164 patients in the building to determine by means of a brief screening method which patients could be considered as possible candidates for open-ward privileges. The only criteria for selection were whether the patient could understand the rules and regulations of open-ward status and whether he would promise that he would obey such rules if given these privileges. This screening process resulted in a group of 123 patients who were considered eligible for the research project. From this original group the experimenters eliminated all patients except those with well-established diagnoses of schizophrenic reaction. Any patient who carried a multiple diagnosis or had an accompanying diagnosis of an organic condition was rejected as a candidate for the program, even though his primary diagnosis was schizophrenic reaction.

In order to test the hypotheses and have adequate control of the experimental variables, it was decided that a minimum of 80 patients was needed, to allow for 16 patients in each of the five experimental groups. When the final group of 80 patients was selected, they were distributed at random within the experimental groups. However, since the patients varied considerably in age and length of hospitalization, it was decided to match the groups as much as possible with respect to these two variables. After the original random distribution, some changing was done to control age and length of hospitalization by placing an equal number of older patients in each of the groups. When this was done, it was found that the mean length of hospitalization for each group was approximately the same without any further changing of the patients in any group. The mean age of the groups ranged from 39.8 to 42.7 years, and the mean length of hospitalization ranged from 9.3 to 12.5 years.

The groups were then identified by letters A through E, only the experimenters having knowledge of which groups were receiving reserpine. This was felt to be necessary so that if any medical problems arose it would be easy to check immediately to see whether the patient was actually receiving the drug. Since the experimenters did not rate any of the patients, it was not felt that this knowledge would bias the evaluation of the effectiveness of the treatment. The following is the identification of the groups and the treatment of each. The groups will be identified by these letters throughout the rest of this paper: (*a*) Group A, reserpine and open ward; (*b*) Group B, placebo and open ward; (*c*) Group C, reserpine and closed ward; (*d*) Group D, no medication and closed ward, (*e*) Group E, no medication and open ward.

The entire project covered a period of six months, which was divided into the following three phases: a two-month preexperimental phase, a three-month experimental phase, and a one-month follow-up period. The preexperimental and follow-up phases were established for the purpose of pre- and postexperimental testing and evaluation of the patients, which will be taken up in more detail later. During the entire six months no changes were made in ward routine, assignments of patients to various activities, transfer to other wards, or ward personnel.

Following the preexperimental period of eight weeks, the patients in the open-ward groups were given full open-ward privileges, and the groups on drugs were started on oral doses of 4 mg. daily. The placebo group was given identical-appearing tablets in the same amount. This procedure was continued for 30 days, at which time the dosage was increased to 8 mg. orally on a daily basis for an additional 60 days.

Methods of Evaluation

From the beginning of the preexperimental phase until the end of the follow-up period, each of the patients was rated weekly by three psychiatric aides on the L-M Fergus Falls Behavior Rating Scale †; weekly blood pressures were taken, and weight was recorded once a month. By this means a base line was established for behavior, weight, and blood pressures before treatment began, and could be followed during the rest of the experiment.

The Minnesota Multiphasic Personality Inventory (MMPI) was administered to each patient during the preexperimental period, and this test was repeated during the follow-up phase.

In recording the behavior ratings for each patient, the mean of the three raters for each item on the scale was used. The mean of all of the patients' scores for each particular behavior item of the scale was then recorded as the group score for comparison among groups. This allowed for a comparison among groups on each of the various kinds of behavior rated, as well as among groups on their over-all behavior.

The statistical tools used were analysis of variance and significance of differences between related means.

Before discussing results, it will be noted that the total number of patients in the analysis of the experimental data do not total the original 80 patients. A few of the patients eloped or wandered around the hospital grounds, disregarding their assignments or not reporting to the ward according to schedule, and were then placed on a closed section; a few of the patients had to be taken from the closed-ward groups and placed on the open section in place of the elopers because the number of closed-ward beds was limited; a few patients were inadvertently shifted to different assignments in the Department of Physical Medicine and Rehabilitation; one elderly patient died of causes unrelated to the experiment, and a few patients became physically ill during the experiment and were dropped from the groups when they were transferred to the general medical ward. For any of the above reasons, or similar ones, these patients were eliminated from the experiment to rule out uncontrolled variables.

In Group A there were three elopements, and one patient became physically ill; in Group B there were two elopements; in Group C six patients were transferred out of the ward; in Group D five patients were transferred, and in Group E there were three elopements and one death. The total number of patients, then, eliminated from the experiment was 21, and this included 8 elopers, 1 who became physically ill, 11 who were transferred, and 1 death. Elopers included not only patients who left the hospital grounds, but also patients who consistently violated the regulations of open-ward privileges, such as not reporting to assignments or not reporting to their wards or meals at prescribed times. Of the original 16 patients in each group, the final number was 12 for Group A, 14 for Group B, 10 for Group C, 11 for Group D, and 12 for Group E, the total being 59 patients. The behavior ratings for these 59 patients were used for comparison among groups on the L-M Fergus Falls Behavior Rating Scale.

The comparison among groups with respect to pre- and postexperimental MMPI profiles necessarily included only those patients in each group who completed the MMPI both times it was administered, and was further limited to those included in the final 59 patients. For the Groups A through E, the numbers, respectively, are 6, 10, 7, 0, and 9, for a total of 32 patients. Of the original 80 patients who were given the MMPI, the respective numbers are 14, 11, 12, 6, and 12, for a total of 55 patients completing the MMPI. Of the 59 patients remaining in the experiment, 40 had completed the MMPI the first time, but there were 4 in Group A, 2 in Group D, and 2 in Group E who would not complete it the second time it was given. One patient in Group B and two patients in Group D finished the MMPI the second time, even though they did not complete it the first time.

Results

1. *Systolic Blood Pressure.*—As can be noted from Figure 1, both drug groups showed a reliable reduction in systolic blood

† References 3 and 4.

pressure, with the placebo group remaining relatively unchanged.

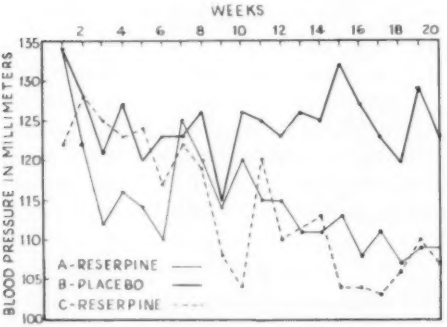

Fig. 1.—Systolic blood pressure.

2. *Diastolic Blood Pressure.*—It can be noted from Figure 2 that there was a reduction in diastolic blood pressure in both the drug groups, with the placebo group again remaining relatively unchanged.

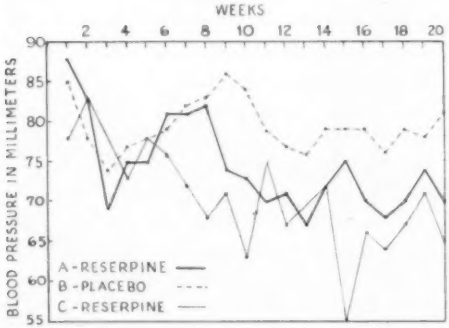

Fig. 2.—Diastolic blood pressure.

3. *Weight.*—The two drug groups gained an average of 4 lb., whereas the placebo group showed an average loss of 3 lb.

4. *Behavior.*—There was no significant change in over-all behavior found in any of the five groups studied as measured by the L-M Fergus Falls Behavior Rating Scale. As can be noted from Figure 3, there is no consistent difference among groups, nor is there any trend toward behavioral improvement perceived in any group that could be attributed to drugs, suggestion, increased attention, or changes in ward routine.

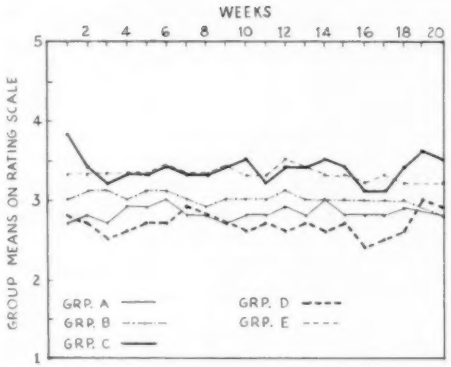

Fig. 3.—Weekly group means on L-M Fergus Falls Behavior Rating Scales.

5. *MMPI Profiles.*—As can be seen on Figures 4, 5, 6, and 7, there were no significant differences found, with one exception, on any of the scales on the MMPI for the groups studied when the pre- and postexperimental profiles were compared. The one exception is a significant increase on the *Hy* score for Group A (reserpine plus open-ward privileges).

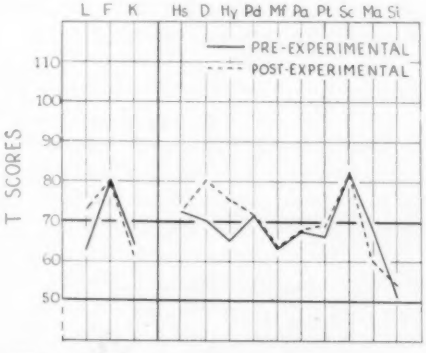

Fig. 4.—MMPI profiles for Group A.

6. *Social Adjustment.*—Open-ward privileges did not result in increased socialization. No significant improvement was found on the scales measuring responses to other patients, psychiatric aides, nurses, doctors, social workers, and psychologists.

7. *Conformity.*—Patients receiving reserpine did not conform better than the placebo and no-medication groups to open-ward rules

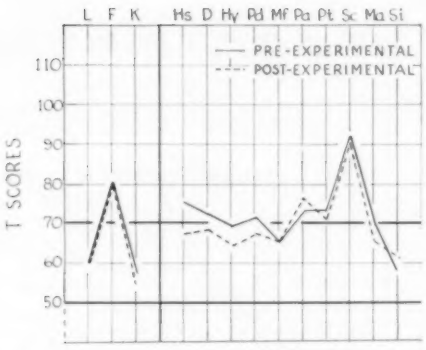

Fig. 5.—MMPI profiles for Group B.

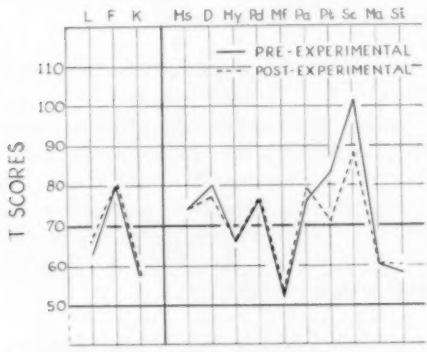

Fig. 6.—MMPI profiles for Group C.

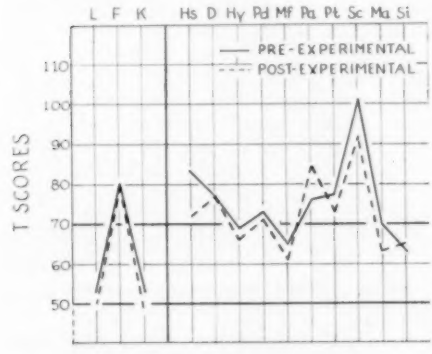

Fig. 7.—MMPI profiles for Group E.

and regulations. Conformity was measured by the number of elopements and by the number of patients who consistently violated the rules of open-ward privileges by such behavior as not reporting to assignments or to their wards or meals at prescribed times. The number of patients falling in this category was eight, and included three in the reserpine group, two in the placebo group, and three in the no-medication group.

8. *Completion of MMPI.*—With respect to the patients who for one reason or another did not complete the MMPI the first time it was administered, it was not found that reserpine resulted in these patients taking it the second time it was given.

Comment

The finding that the use of reserpine resulted in a reliable reduction of both systolic and diastolic blood pressure is consistent with the findings of other investigators. In addition, as was found in another study,[8] reserpine tended to bring about a slight gain in weight, while the placebo group showed a slight loss in weight. We can offer no explanation to explain this loss of weight with placebo tablets.

The negative results with respect to improvement either behaviorally or as measured by the MMPI may be due to several factors. First, 8 mg. orally per day may not be an effective dosage for chronic schizophrenic patients. Second, reserpine may not have a generalized therapeutic effect on such chronically disturbed patients. Third, the administration of the drug may not have been continued over a sufficient time to obtain positive results. As to the amount of the drug given to the patients, it compared very favorably with the dose given by other experimenters who have reported positive results, and in many cases was considerably more than has been given by others.

As part of the original design, we planned to administer the drug for a period of 90 days. As a result of surveying the literature for previously reported studies of the use of reserpine, it seemed reasonable to assume that positive changes in behavior, if they were to occur, would begin to manifest themselves within this period of time.

We also decided to check results at the end of the 90-day period, and, if some improved behavior was observed, to continue the drug for a longer period. Since no changes were noted, it is our opinion that three months on the drug was a sufficient test of its effectiveness. We feel that reserpine given at random to chronic schizophrenics is of little effectiveness, and that further research should be directed toward the development of a set of criteria to be used for the selection of patients who might profit from such treatment.

Although other studies have indicated that increased attention, changes in ward routine, and suggestion have resulted in improvement of behavior, this was not found in this study. We feel that such factors were kept to a minimum in this study, since ward activities were unchanged and all of the patients were already assigned to various activities that kept them busy during the day. The number of ward personnel was not increased, and they were instructed not to show any increased attention to the patients or to comment on the purpose of the drugs.

No harmful side-effects were noticed with the use of reserpine, except in one patient who developed a Parkinson-like syndrome. This disappeared upon discontinuance of the drug.

As has been pointed out, not all the patients completed the MMPI; so it was not possible to compare the MMPI profiles of all the patients in each of the groups. Failure to complete the MMPI was attributed to several things, including negativism and hostility, confusion, and inability to understand directions; a few patients were mute and would not attempt to answer or look at any of the cards, and a few sat in front of the MMPI boxes apparently hallucinating constantly. Some of these patients spent as long as three days on the test without completing it; so further attempts at testing were discontinued. The only change in the MMPI profiles which was significant at the 0.05 level was an increase on the *Hy* scale for Group A, and this finding might be expected to occur by chance when the total number of comparisons made is considered.

The granting of open-ward privileges to chronic schizophrenic patients who have been on a locked ward for a number of years did not seem to have any positive effect on their behavior. It did not result in increased socialization or improved interpersonal relationships, and it did not seem to serve as a reward or as an incentive to change their behavior in a more socially acceptable direction. Patients who were not reporting to their assignments or to the ward at prescribed times were warned about the possible loss of their privileges, but this did not seem to be effective in changing their behavior. As mentioned previously, patients in open-ward groups who violated the rules and regulations of open-ward privileges were returned to locked sections and were dropped from the experiment. However, weekly ratings of them were continued, and these ratings did not indicate any negative change in behavior as a result of the loss of open-ward privileges. This raises the question as to whether being placed on an open ward is very meaningful and rewarding to patients similar to those used in this experiment. It suggests that awarding of open-ward privileges is insufficient to produce improved behavior, and that such a change in ward status should be utilized in conjunction with a total-push type of program, which can usually be more effectively used with open-ward patients.

One of the most interesting results of the experiment is the discovery that even with such a crude screening method as was used in this study potential elopers could be reduced to a minimum. Of the total number of eight listed as "elopers," only three actually left the hospital grounds. One of these was picked up by hospital personnel; one called the hospital from a nearby railroad depot to ask to be returned to the hospital, and one went to his home. The parents of this patient called the hospital to report his arrival and to request that they be allowed to keep him with them.

This finding would suggest that many of the other patients in the hospital who have been on locked wards for many years could be placed on open wards, or that many of the locked wards could be changed to open ones. At the present time 45% of the patients in this hospital are on open wards, and it is planned to increase this percentage despite the findings of this study that open-ward privileges per se are not sufficient to produce desired changes in chronic schizophrenics. There are several reasons for this planned change. First, there would be a lessening of some of the administrative problems on the ward. An obvious example is the reduction of time spent by the psychiatric aides in transporting patients to the various activities in other sections of the hospital. Second, it would make available to the patients many activities which are therapeutic but which are not available to closed-ward patients because of the number of personnel that would be required for supervision. This applied especially to the many recreation activities that are conducted on the hospital grounds. Third, the opening of the ward for this study resulted in greatly increased morale of the personnel members on the ward. They no longer felt that they were working on one of the "hopeless" or "back" wards in the hospital, or that nobody was paying any attention to what was going on in their building. Fourth, it would mean a gain in the number of open-ward beds in the hospital and would reduce some of the "waiting time" of patients on closed wards until open-ward beds were available.

Summary

Eighty chronic schizophrenic patients on a closed ward were divided into five groups of 16 patients each. One group was given reserpine and open-ward privileges; one group was given open-ward privileges without medication; one group was given open-ward privileges and placebo; one group remained on a locked section and was given reserpine, and one group remained on the locked section without medication. The drug groups were given 4 mg. orally each day for 30 days, and this was increased to 8 mg. orally per day for the next 60 days. The placebo group was given identical-appearing placebos in the same amount. All groups were studied for eight weeks prior to and for four weeks subsequent to this period of 90 days. Weekly ratings of behavior were made throughout the entire six months, and the Minnesota Multiphasic Personality Inventory was given before and after the three-month period of medication. Measurements were made of blood pressure and weight at regular intervals.

Conclusions

1. Reserpine in oral doses of 8 mg. per day did not result in improvement, as measured by rating scales and by the MMPI, in chronic schizophrenic patients.

2. Patients receiving reserpine did not adjust better on the open ward than patients receiving no medication, as measured by conformity to the rules of the ward and the number of elopement.

3. Awarding of open-ward privileges did not result in improved interpersonal relationships or behavioral improvement.

4. Reserpine did effect a lowering of blood pressure.

5. Reserpine resulted in a slight weight gain.

The Upjohn Company furnished us with the placebo; C. Lewis, M.D., Manager, authorized the project; W. B. Hall, M.D., ward physician, cooperated and assisted in setting up the project on his ward, and all the nurses on the ward assisted. Psychiatric aides rated the patients throughout the entire experiment.

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Progression of Effects of Lysergic Acid Diethylamide [LSD]

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Introduction

Since the Swiss chemist Hoffman, on April 16, 1943, accidentally discovered the mental effects of lysergic acid diethylamide (LSD-25), a great many experiments with the drug have been reported in various journals. Observations show most agreement in the area of physical subjective symptoms and unreality and least agreement in changes of mood and behavior.

Tremor, nausea, dilation of pupils, perspiration, and changes in blood pressure have been consistently found. The observed mental effects have been more at variance. Busch and Johnson,[1] interested in LSD-25 as a possible therapeutic agent, have found it to cause increased activity, exhibition of emotion, and expression of psychopathology, with only short periods of confusion and occasional visual hallucinations. Similarly, Sandison, Spencer, and Whitelaw[2] emphasize reliving of repressed personal experiences resulting from nonselective disturbance of the unconscious. Savage,[3] in a clinical psychological study, has found the mood to be one of aggrandizement, omnipotence, and euphoria with hallucinations frequent, while in a later analytic study[4] he emphasizes hallucinations and ego disturbances, suggesting that loss of ego feeling progresses from legs and genitals to arms and trunk, affecting the face and lips (first to be included in the ego) last. Hoch, Cattell, and Pennes,[5] comparing the effects of mescaline and lysergic acid on three groups of patients, report a wider variety of changes than other authors as effects of LSD, finding perceptual alteration in the foreground with visual illusions and hallucinations very common. Although there is a tendency to disinhibition and increased psychomotor activity, there is also found a comfortable lassitude and sedative effect. These authors found that the emotionality of the reaction varied with their three groups, being most intense with pseudoneurotic schizophrenics and least intense with deteriorated schizophrenics.

DeShon, Rinkel, and Solomon,[6] doing a complete psychiatric assessment and working with normals, found that indifference and blunting were protracted, with suspiciousness and hostility transient, that behavior was characterized chiefly by underactivity and lack of spontaneity, that disturbances of perception were mostly of the illusional type, and that depersonalization, as well as hallucinations, when present, was closely related to feelings of unreality.

Noting the inconsistencies and lack of agreement, Abramson and associates[7] investigated statistically the answers of normal subjects to a list of symptoms. They report that there are significant increases in the number of normal subjects responding with zero, 50γ and 100γ of LSD. The authors add the suggestion that the subjective quality of a symptom with 100γ may well be different from that of the same symptom reported with placebo.

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Among the diverse reports, some writers have conceptualized the effects of LSD and related drugs by invoking ego psychology. Thus, Lindemann and Clarke,[8] on the assumption that drugs produce changes in the integrative functions of the ego, go on to enumerate the changes caused by different drugs. Personality has not been systematically explored as a variable in reaction to the same drug, but has been alluded to by Hoch,[5] who found differences in the reactions of his patient groups, and by Savage,[3] who points out that distortions of reality may be accompanied by either euphoria or anxiety.

In general, we say that the discrepancies in observation are not surprising, considering that the reports on LSD refer to patients as well as normals, and to different doses of the same drug and that they are fitted into different conceptual frameworks for economical purposes. The dosage factor may partially account for the lack of agreement in general, and specifically for the findings of Sloane and Lovett Doust [9] of no measurable impairment or change in several psychological functions. They administered only 40γ to their normal subjects, whereas in the Boston Psychopathic Hospital [6] and Mount Sinai Hospital [7] reports of positive findings larger doses were used.

Moreover, the importance of the attitude of the experimenter and of other people interacting with the subject tends to be consistently minimzed. Hyde [10] has shown that the affective interplay of subjects and experimenters has a mirror effect; that the strong affective relationships of hostility and affiliation are distorted much more frequently than the impersonal, empathic, and nurturant interplay, and, further, that qualitatively the type of distortion corresponds to the type of affect. Bockoven,* stimulated by Hyde's findings and attempting a comprehensive search for the effects of LSD, has stated that when the results are studied from the larger perspective of social psychology scarcely any specific psychological effects can be identified which cannot be better accounted for in terms of social factors.

The preceding review demonstrates the existing need for a clearer documentation of the LSD syndrome. Clinical evaluation without agreement as to the categories or functions to be evaluated plus lack of definitions lead to apparently discrepant observations, on the one hand, while the perspective of social psychology, dealing with the multiplicities of interpersonal relations, tends to confound the direct effects of the drug by absorption into the social matrix. On the basis of our experiments, it is felt that differences in dosage and phase of the LSD reaction observed account for many of the discrepancies. The purpose of this paper is to identify a progression of phases in the LSD reaction at our standard dose level.† Through this, it will be seen that certain apparent discrepancies in the comparison of other studies may be reevaluated.

Method

The literature is in general agreement that the subject reports symptoms within 30 minutes after ingestion of LSD-25 and that cessation occurs within 12 hours. DeShon [6] and associates describe three major phases, lasting 12 to 16 hours, and a fourth phase, of mild after-effects, lasting for several days. The first phase was the period of administration of the drug to the height of the reaction. The second phase was the height of the reaction,

* Bockoven, J. S.: Effects of Social Situations on the Quality of Interpersonal Relations and Symptom Intensity in Lysergic Acid Psychosis, 1953 Annual Report to Geschickter Foundation.

† Our standard does is 1γ per kilogram of body weight.

lying within a time span of one to five hours, and the third phase, the period from the end of the height of the reaction until evening, was characterized by reduced activity, poverty of thought, indifference, and flat affect. The height of the reaction occurring rarely after five hours, onset, peak, and decline are included in the present observations by listing symptoms for a period of eight hours.

The data used in this study were the observer's notes. During the experimental day, the subject was accompanied by a trained observer, who recorded, verbatim, the subject's conversation with others, his facial expression, posture, and motor responses. The protocols used were those of the first 20 experiments on 18 normal subjects receiving 1γ per kilogram of body weight. Symptoms were classified from the observer's protocols for each hour of the eight-hour period according to the criteria of peculiarity, intensity, duration, and frequency.

Having been impressed by the penchant of LSD experimenters to use "objective" techniques and categories and to concentrate on hallucinations, delusions, depersonalization, and other pathological segments, we decided to define our symptom groups in terms of the bipolar relation of subject and environment, thus not precluding "normal" behavior from our results. Our symptom groups, with their rationale, follow:

1. Gregariousness: verbalized sexual desire, elation, friendliness, giddiness—intoxication symptoms which dissipate subject's affect into acceptable social channels
2. Anxiety and Apprehension: symptoms of affective quality wherein the subject contains his affect
3. Irritation and Hostility: symptoms which mediate communication of subject's affect to his environment
4. Neuromuscular symptoms: heaviness, restlessness, tenseness, weakness, tremulousness, fatigue
5. Cutaneovascular symptoms: perspiration, cold, warmth, numbness, tingling, and dizziness
6. Awayness: apathy, depression, indifference, lethargy, seclusiveness, disinclination to talk, lassitude—symptoms indicating that expression of affect is not overtly sought
7. Confusion of Thought: tearfulness, suspiciousness, perplexity, ambivalence — severe, subjectively incapacitating symptoms
8. Perceptual Distortion: visual misperception of the environment, especially of other people
9. Unreality: inexplicable pervasive feelings of strangeness, accompanied by acceleration or cessation of time, loss of reality, in some subjects exacerbated by anxiety
10. Inappropriate Laughter and Smiling: inadvertent communication to the environment of involuntary affect

Equivalence; Disparity; Apology

In presenting our results, we are faced with the possibility of either recording the number of symptoms in each category or indicating the hour of maximal symptoms for a category as a norm and the remaining hours as percentages of the maximum. We chose the latter course. The rationale for such presentation stems from the disparity of number and type of symptoms in the various groups, which, when plotted by number alone, would give the impression of physical dysfunction as the main action of LSD. While Neuromuscular and Cutaneovascular symptoms would seem paramount in the symptom picture, Unreality and Perceptual Distortion would appear to be of minor importance when only numerical incidences are considered. The latter symptoms, however, are among the most unique reactions caused by the drug. A symptom entered under Unreality must be of relatively protracted duration and would be entered only once in a time period; those of the physical type are often momentary and usually have several entries in a time period. By representing the frequency of each category of symptoms in any hour as a percentage of the frequency in a maximal hour, we relate the frequency of each symptom hour to its own norm and, at the same

time, provide a quantitative basis for comparison with other symptoms.

Results

Gregariousness (Fig. 1), a "normal" and acceptable outlet, is at a maximum during the first hour after the ingestion of LSD. It declines slowly but steadily until the fifth hour, before it rises in the third and fourth hours, at which time the effects of LSD are felt most intensively by the subjects.‡ Here it must be noted that this symptom group denotes an unpleasant affect, of which the subject has awareness. It is of significance, then, that awareness of Anxiety and Apprehension is marked in the first hour, when LSD effects are neither very

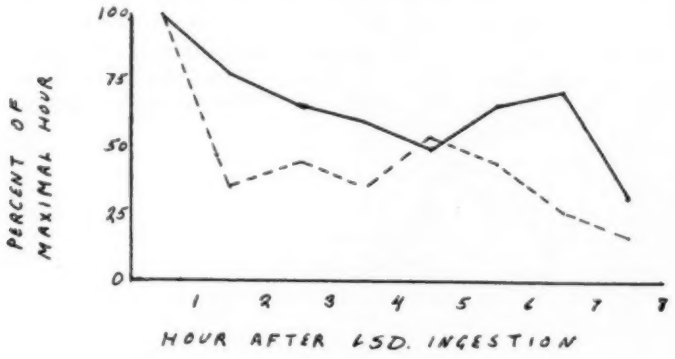

Fig. 1.—Gregariousness (solid line), and anxiety and appreciation (broken line).

Fig. 2.—Hostility.

the sixth and seventh hours. This type of expression does not fall below 50% of maximum, indicating that even under the most unusual of stresses some subjects are still able to channel some energy into appropriate outlets.

The syndrome of Anxiety and Apprehension (Fig. 1) is similar to Gregariousness insofar as it has its peak in the first hour. The drop in the second hour, however, is marked and remains low in noticeable nor very marked. There is a slight tendency for Anxiety and Apprehension to increase in the fifth hour, before the syndrome again declines toward the end of the day.

Irritation and Hostility are also normal outlets, and we would expect them to follow the pattern of the previous

‡ Morimoto, K.: Subjective Graphic Study of LSD Symptom Intensity, 1953 Annual Report to Geschickter Foundation.

two groups. A satisfactory explanation of the divergence of this symptom group from the form of the rest of the "normal" processes (Gregariousness and Anxiety) entailed a minute search of protocols. The subject, confronted with a psychotic experience and in the midst of experimenters and authority figures, would not be expected to show hostility.[11] For the most part this is the case, since as a group of symptoms the count at its maximal hour is smaller than that of any group, with the exception of Inappropriate Laughter and Smiling. Further, probing into the protocols reveals that in our experimental situation hostility has an inverse relationship to anxiety; i.e., anxious subjects were least likely to be hostile. Situationally, our subjects are encouraged to relate by reporting experiences and symptoms to the experimenters. In refractory subjects this pressure to relate is countered by hostility and suppression of psychotic phenomena.

Neuromuscular symptoms (Fig. 3) are observed in great quantity during the first hour of LSD psychosis. They attain a maximal peak in the second hour, followed by a sharp decline in the third hour and gradual decline thereafter. Symptoms of the Cutaneovascular variety adhere to a very similar pattern. They have a large relative frequency in the first hour, reach a peak in the second hour, drop sharply in the third hour, and wane gradually from the fourth hour onward.

Neuromuscular and Cutaneovascular symptoms are most often considered the physical correlates of anxiety and/or tension, and may also be regarded as the beginning phases of depersonalization.[12] In these results, they are the first symptoms which the subject reports as drug-induced changes and appear along with the Gregariousness and Anxiety.

The symptom group termed Awayness (Fig. 4) has a remarkable growth in the second hour. The nonrelation or lack of interpersonal processes signified by the appellation is seen only sporadically in the first hour, when the physical symptoms have been found to be already present in quantity. In the second hour, this type of behavior is trebled and shows a slight increase in the third hour, at which time somatic complaints are considerably reduced. Of note here is the trough in the fifth hour, which will interest us later. Awayness has both adjustive and maladjustive components, for it may be used as a strategic withdrawal from interaction in order to arrive at a satisfactory solution of complex interpersonal processes, or it may reflect a passive, inferior adaptation of one's resources, which, in its extreme, is viewed as a psychological death. In this context, the relation of Thought Confusion to Away-

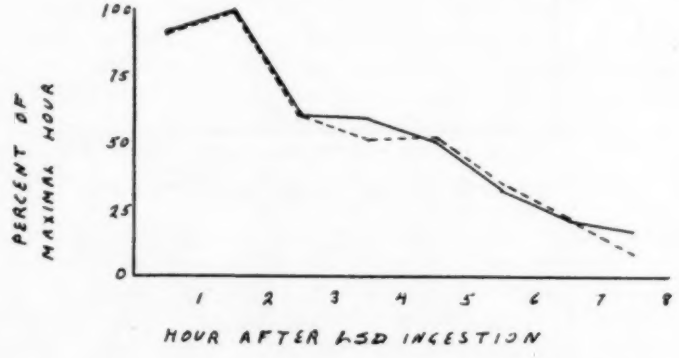

Fig. 3.—Neuromuscular symptoms (solid line) and cutaneovascular symptoms (broken line).

ness (Fig. 4) is regarded as significant; failure of intrapsychic mastery or conflict about utilization of this withdrawal defense results in Thought Confusion in some subjects. It would seem implied that attempts at symbolic mastery (Awayness) of a stressful situation results in the subjectively crippling symptoms of Thought Confusion.

The frequency of Inappropriate Laughter and Smiling (Fig. 6) is small, but its relationship to Anxiety and Hostility shall be discussed, for the dichotomy of anxious and hostile subjects yields a correlation indicative of personality types. In our group of anxious subjects, Inappropriate Laughter and Smiling has an inverse relationship to Hostility. As

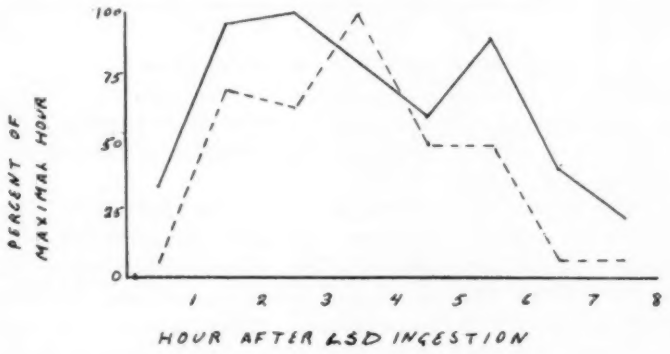

Fig. 4.—Awayness (solid line) and thought confusion (broken line).

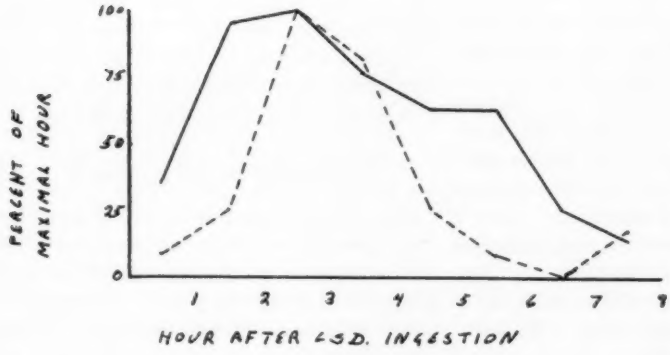

Fig. 5.—Perceptual distortion (solid line) and unreality (broken line).

Perceptual Distortion, like Awayness, has a sharp increase in the second hour and is maintained high up to and including the sixth hour. Pervasive feelings of unreality are almost absent in the second hour, but rapidly increase to a maximum in the third hour, remain high in the fourth hour, but wane fast in the fifth hour. Unreality seems to lag Perceptual Distortion in the same manner that Thought Confusion follows Awayness.

laughter increased, in the fourth hour, hostility decreased; as hostility increased, in the fifth hour, laughter dropped out entirely, and as laughter increased, in the sixth hour, hostility again decreased. In the hostile subjects the relationship is positive. In this group both Hostility and Inappropriate Laughter and Smiling reached a peak in the third hour and a trough in the fourth and fifth hours. The anxious subject is aware of his need of reassurance from the observer

Fig. 6.—Inappropriate laughter and smiling.

and cannot, therefore, be rejecting of him.

In Figure 7 related symptom groups are shown together. The major discrepancy of form occurs in the non-normal, nonsomatic symptoms at the fifth hour. Examination of the decrease and increase of these symptom groups reveals that the decrease of Unreality in the fifth hour is accompanied by a decrease in Awayness, Thought Confusion, and Inappropriate Laughter and Smiling. The increased or same normal processes, at this same hour, would lead us to believe that the psychotic experience was over and that integration of said experiences was being made. However, the somatic processes and perceptual distortion in the hour are unchanged, indicating that the subject is still giving reality to unreal experiences (Perceptual Distortion) or somatizing affect (physical symptoms). The subject's apparent integration of the lysergic experience is premature.

The relapse in the sixth hour substantiates the thesis of premature integration. The subject, again aware of strange and alien sensations, becomes preoccupied. Other people's actions being incongrous with his internal orientation, he responds with inappropriate laughter and smiling. Conversely, the subject's attempt to behave normally in the fourth and fifth hours is reflected by a decrease of inappropriate outbursts.

Consolidation and Comment

The presentation was influenced by two overlapping factors: the hour that the symptom group was maximal and the type of symptom groups. Gregariousness, Anxiety and Apprehension, Irrita-

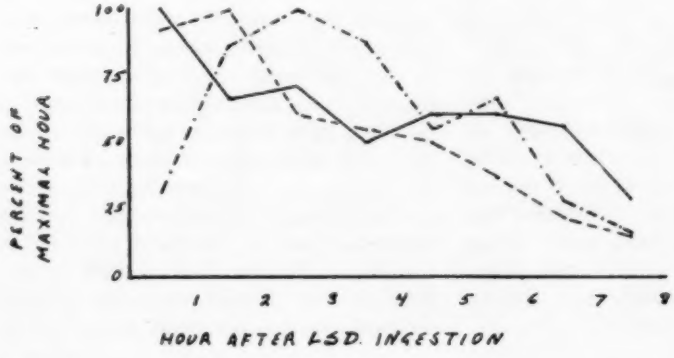

Fig. 7.—Normal: gregariousness, anxiety, hostility (solid line). Somatic: neuromuscular and cutaneovascular (broken line). Abnormal nonsomatic: awayness, thought confusion, inappropriate laughter and smiling, perceptual distortion, unreality (line of dots and dashes).

TABLE 1.—*Percentages for the Seven Figures*

Hour	1	2	3	4	5	6	7	8
Figure 1								
Gregariousness	100	78	67	61	50	67	72	33
Anxiety and apprehension	100	36	45	36	55	45	27	18
Figure 2								
Hostility	78	67	100	33	78	56	44	22
Figure 3								
Neuromuscular symptoms	92	100	61	59	51	33	22	18
Cutaneovascular symptoms	91	100	61	52	52	35	22	9
Figure 4								
Thought confusion	7	71	64	100	50	50	7	7
Awayness	35	96	100	81	62	91	42	23
Figure 5								
Perceptual distortion	36	95	100	77	64	64	27	14
Unreality	9	27	100	82	27	9	0	18
Figure 6								
Inappropriate laughter and smiling	71	86	100	71	14	57	43	0
Figure 7								
Normal	100	67	72	50	61	61	56	28
Somatic	92	100	61	55	50	37	22	15
Abnormal Nonsomatic	32	87	100	88	55	67	28	16

tion and Hostility (Figs. 1 and 2) form a syndrome which is familiar to our everyday experience; they can be found in a normal sampling of people going through their routine activities. The first two mentioned manifestations of normal behavior are at a peak immediately after the ingestion of the drug, while Irritation and Hostility is seen infrequently, and only in a minority of subjects. The subject placed in a novel social situation of experimental design and faced with the prospect of a psychotic experience can be said to be appropriately friendly, appropriately anxious, and minimally hostile. This is a pattern of behavior most conducive to securing nurturance and affiliation and warding off unpleasant action. As the drug becomes effective, other patterns become operative.

The second set of symptom groups which cluster together under a wider category are the Neuromuscular and Cutaneovascular symptoms, as shown in Figure 3. These physical signs are the first indication which the observer has that an abnormal process may be taking place in the subject. Somatic phenomena occur with great frequency in the first hour and are most marked in the second hour. Gregariousness, and Anxiety and Apprehension are declining in the second hour, while Neuromuscular and Cutaneovascular symptoms are increasing. It could be said that the latter represent anxiety equivalents and, broader, affect equivalents.[12] Physical signs and symptoms, often regarded as neurotic, may also be the normal response of the subject to a stressful situation.[13] As other types of symptoms appear in the third hour, somatic signs are less numerous but are maintained until the fifth hour.

The third set of symptoms is considered ideational, or internalized (Fig. 4). The subjective rumination and withdrawal of the Awayness symptoms may result in confusion, manifested by paranoid ideas or exaggerated emotional outlet, such as crying. The extended peaks of the Awayness and Thought Confusion groups overlap, and in some subjects these symptoms overshadow the peaks of somatic dysfunction, Perceptual Distortion, and Unreality. Any and all of the latter may serve to precipitate Away-

ness and Thought Confusion, which, in turn, may serve to conceal what both subject and observer regard as psychotic phenomena (Distortions and Unreality).

The fourth set of symptoms consists of Perceptual Distortion and feelings of Unreality (Fig. 5). Having in common a perceptual element, these two differ in that the former is customarily unaccompanied by affect, perhaps being an ego defense against the recognition of inadmissible impulses and emotions, while the latter goes by the feelings of unreality. Perceptual Distortions and Unreality are both at a peak in the third hour, but Unreality stays high in the fourth hour, thus indicating possibly that after a final attempt to ward off objectionable feelings by somatizing, mentalizing, and misperceiving the reality of situations, the objectionable impulses and affects are again felt clouded in the aura of unreality.

TABLE 2.—*Peaks of Symptom Groups*

Symptom Class	Hour of Peak
Normal	1
Gregariousness	
Anxiety	
Hostility	
Somatic	2
Neuromuscular	
Cutaneovascular	
Abnormal Nonsomatic	3
Awayness	
Thought Confusion	
Perceptual Distortion	
Unreality	
Inappropriate Laughter and Smiling	

In summary, the peak of the symptom group is later in time as we proceed from normal behavior to somatic dysfunction to mental and perceptual aberration (Table 2 and Fig. 7). Normal behavior overlaps and appears to be supplanted by physical complaints, which, in turn, give way to ideational preoccupation, distortions of reality, and unreality feelings. The impression is that a cycle is completed by the return of affect.

Conclusion

In our introduction we listed points of view. Some workers emphasized the therapeutic possibilities of LSD; others focused attention on hallucinatory, delusional, and depersonalization material. Our own results, undoubtedly influenced by the schema selected to condense the raw data, resulted in a differential progression of variously rationalized groups. We then interpreted the progression of groups as the substitution of diverse mechanisms as a method of warding off objectionable feelings and impulses. Whether the progression of such mechanisms can be manipulated toward therapeutic ends cannot be resolved from these observations. Additionally, personality factors and situational determinants must be considered.

Hyde [10] has shown that exacerbation or alleviation of symptoms in the lysergic psychosis is partially dependent on the situation of which the subject is a part and that the subject's perceptions (hallucinations and delusions) are conditioned by the attitudes and feelings of those people with whom he interacts.

Bockoven's point of view,§ that as the lysergic symptoms are analyzed in the context of social psychology they seem to take meaning as adaptive to the situation, is pertinent. As the observer removes himself from his fixed point of reference and analyzes the total situation for its import on the lysergized subject, he understands that what on the surface may appear as hallucination and delusion may actually turn out to be a penetrating insight or perception the meaning of which may not be apparent to either subject or observer.

We conclude that the progression of mechanisms seen with LSD may be used either as a means of observing and dis-

§ Bockoven, J. S.: Effects of Social Situations on the Quality of Interpersonal Relations and Symptom Intensity in Lysergic Acid Psychosis, 1953 Annual Report to Geschickter Foundation.

playing curious "pathological" phenomena or as a therapeutic aid in making defense mechanisms available for scrutiny to subject and therapist. The purpose served will depend upon the skill, inclination, understanding, and intention of both subject and observer.

Summary

After summarizing some of the lysergic literature and the need for documentation of the LSD syndrome demonstrated, we defined 10 symptom groups in terms of the bipolar relationship of subject and environment.

A step-like progression is noted in our results:

1. Normal processes of Gregariousness and Anxiety and Apprehension are most marked in the first hour, when the drug action is not fully effective.

2. Somatic symptoms appear in the first hour, reaching a peak in the second hour.

3. Perceptual Distortion, present in the first hour, increases in the second hour and is at a peak in the third hour.

4. Unreality is at a peak in the third hour and is well maintained in the fourth hour.

5. Awayness or ideational phenomena accompany the preceding processes from the second to the sixth hour.

6. Thought Confusion, with its peak at the fourth hour, is interpreted as the break through when attempts at intrapsychic mastery of stressful situations, as indicated by the Awayness phenomena, fail.

7. The trough, in the fifth hour, of Awayness is seen as a premature attempt to integrate the experience and behave normally.

[The hypothesis is offered that objectionable impulses and feelings are warded off progressively by diverse mechanisms. Somatization of affect may be succeeded by misperception of reality and feelings of unreality, while preoccupation in the mental sphere may accompany any of these processes. A cycle seems to be completed with the return of feelings of unreality.]

8. After the sixth hour, all symptom groups, with minor exceptions, show a general decline.

Therapeutic potentialities of LSD are mentioned.

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Behavioral Evaluation of Chronic Mental Hospital Patients Treated with Reserpine

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Introduction

Reserpine,* a pure crystalline alkaloid of Rauwolfia, has received considerable attention by psychiatrists during the past two years. Although initial clinical studies were designed to demonstrate its effectiveness in producing mild, sustained lowering of blood pressure, the literature now commonly reports the drug to have a tranquilizing effect on patients with psychoneurosis, as well as producing "marked improvement" in such mental diseases as schizophrenia, paranoia, manic status, and dementia paralytica and in some cases of depression.

The enthusiasm with which many rechronic mental hospital patients has been noted. Hollister and associates [1] report "unequivocal" improvement in 6 of 19 patients receiving 2 mg. of reserpine orally for 50 days. (The basis for evaluation is not clear.) Campden-Main and Wegielski [2] report a definite "reserpine effect" at the end of an experimental period in which the oral dosage was as little as 3 mg. of reserpine per day. Behavioral changes were measured by the Ferguson Hospital Adjustment Scale.† Others (Noce and Williams [3] and Kline [4]), using less objective measures of behavioral changes, have obtained searchers have reported results with "dramatic" results with minimal dosages (less than 4 mg. per day).

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* The supply of reserpine (Serpasil) was courteously supplied by the Research Department, Ciba Pharmaceutical Products, Inc., Summit, N. J.

† Ballachey, E. L.; Ferguson, J. T., and McReynolds, P.: Hospital Adjustment Scale for Evaluating Patients' Behavior in a Psychiatric Hospital, 1951.

Purpose of Study

With certain of the above-mentioned observations providing the stimulus, the present study was formulated with the following specific purposes in view:

1. To evaluate the effect of reserpine with respect to the practicality of its use on a so-called chronic ward in a state mental hospital. This would involve oral administration of the drug for the sake of convenience and a minimal dosage of the drug for the sake of economy (availability of personnel and the cost to us to be of paramount consideration in the practical use of the drug).

2. To evaluate the effect of reserpine through the use of an experimental design and method of measurement which would greatly minimize the effect of any personal investment or bias on the part of persons directly or indirectly connected with the research. It is felt that this aspect of experimental design has been rather blatantly neglected in certain studies recently published.

3. To determine the effect of increased dosage of reserpine in accelerating any changes which might be taking place in the patient's behavior.

Selection of Subjects

1. The patients were selected from a so-called "back ward" of a state hospital receiving all types

of mental patients (St. Peter State Hospital). The building from which the subjects were selected housed approximately 350 regressed female patients.

2. All patients at this hospital are annually rated independently by two raters on the L-M Fergus Falls Behavior Rating Scale[5] (L-M Scale). The average ratings for the past three years were obtained, and the patients were selected (through I. B. M. tabulating equipment) with respect to their over-all ward behavior. The L-M Scale is a five-point scale measuring behavior in 11 different areas of day-to-day ward behavior, e.g., work, response to meals, response to other patients, psychomotor activity, speech, toilet behavior, etc. It uses relatively simple terms and does not require the rater to make any inferences above the simple behavioral level. It was designed with the objectives of sensitivity to behavioral change, adequacy of behavioral sample, and rapidity of rating. It is sufficiently reliable and objective to minimize the effect of the raters' subjective "feelings" on their ratings.

3. All patients over the age of 65 were eliminated, and all patients were dropped whose illness might be attributed to central nervous system syphilis or other clear-cut organic diseases.

4. One hundred patients with the lowest (poorest behavior) scores on the L-M Scale for the past three years were then selected. Of these, 50 were selected on the basis of aggressiveness and other behavior classified as "overactive."

5. These patients were randomly divided into two groups—one to be used as the experimental group and the other to be used as a control group. No significant differences existed between these two groups with respect to age, length of hospitalization, diagnosis, or score on the L-M Scale.

Procedure

1. The designation of Group A as the experimental group (receiving reserpine) and of Group B as the control group (receiving placebo tablets identical in size and markings) was made by the superintendent of the hospital, all others being unaware of this designation.

2. All patients were rated independently by two raters on the L-M Scale one week prior to the beginning of the administration of the drug, and weekly thereafter. These raters were registered nurses or psychiatric aides who had been in personal contact with the patients for some time and who felt comfortable in using the scale.

3. Prior to the beginning date of the administration of the drug, each patient was evaluated by two psychologists and a physician. The observations made at this time were put in objective form through the use of the Lorr-Jenkins Multidimensional Scale for Rating Psychiatric Patients, hereafter referred to as the MSRPP.[6]

The Multidimensional Scale for Rating Psychiatric Patients, Hospital Form (MSRPP) is a schedule of 62 brief rating scales, 52 of which may be scored on the factors: (*a*) retarded depression *vs.* manic excitement, (*b*) compliance *vs.* resistiveness, (*c*) paranoid projection, (*d*) activity level, (*e*) melancholy agitation, (*f*) perceptual distortion, (*g*) motor disturbances, (*h*) submissiveness *vs.* belligerance, (*i*) withdrawal, (*j*) self-depreciation *vs.* grandiose expansiveness, and (*k*) conceptual disorganization. The schedule is designed so that 40 of the scales are rated by psychiatrists or psychologists, and the remainder are rated by ward personnel. The authors of the schedule state in their manual: "The schedule secures in a relatively objective and quantitative form a description of the observable behavior or readily inferrable traits and common symptoms of hospitalized patients. The scales represent a broad sample of important symptoms characteristic of the functional psychoses. They demand a minimum of interpretation on the part of the observer and they yield judgments relatively unbiased by the rater's point of view or theoretical persuasion."‡

4. For a period of two months the experimental group received, orally, 1 mg. of reserpine, b.i.d. The control group was given placebo in identical fashion. Each week during this period all patients were rated independently on the L-M Scale by an aide and a nurse.

5. At the end of the first two-month period the dose was doubled, and for a period of three months thereafter the patients in Group A received 2 mg. of reserpine, b.i.d., and those in Group B identical amounts of placebo. During this period biweekly ratings were obtained on the L-M Scale by independent raters.

6. At the end of the treatment period all patients were again evaluated by the same two psychologists and physician with the MSRPP.

7. At no time did any person working either directly or indirectly with the research know the identity of the two groups.

8. Since the ward physician was unaware of the identity of the test and control groups, it was necessary to include in the experimental design the provision that any patient might be dropped from the study if the physician felt that their physical well-being was threatened.

Results

In the course of the study the physical condition of certain patients became such that the ward physician felt that medication should be discontinued, and they

‡ Lorr and others,[6] p. 1.

were dropped from the study. During the first half of the experimental period, one subject was dropped from the control group and two were dropped from the experimental group. During the last half of the experimental period, one additional subject was dropped from the control group and seven additional subjects were dropped from the experimental group, making a total of 23 controls and 16 experimental subjects to survive the entire experiment. Upon statistical examination, no difference of significant magnitude was found to exist on the L-M Scale between the 16 surviving experimental subjects and the 7 dropped experimental subjects in response to the first 10 weeks of medication.

After establishing the comparability of the test and the control group on both rating instruments and testing for homogeneity of variance, the *t* test was used to determine the significance of the mean differences between ratings.§ On the MSRPP, the mean differences between the initial and the final ratings on all factors, as well as the total score or "morbidity score," were used. On the L-M Scale, the total scores of each of three ratings were compared—the initial rating, made immediately prior to the first administration of the medication; the midpoint rating, made immediately prior to doubling the dose, and the final rating, made at the end of the experimental period. The mean difference of the various ratings of the test and control groups on both the MSRPP and the L-M Scale were compared for statistical significance.‖

Upon examining the data, it was found that none of the mean differences were of sufficient magnitude to be of "conclusive" significance. As a consequence, the following comments concerning changes in behavior, as measured by the MSRPP and the L-M Scale, are to be regarded as only "suggestive" evidence in favor of the medication.

The MSRPP.—Upon examination of the differences in response to medication by the test and the control group, differences of "suggestive" significance were found on the factors compliance-resistiveness and activity level, as well as on total score, or "morbidity score." The test group appeared to become slightly more compliant and to become slightly less active, whereas the controls remained unchanged. The over-all adjustment of the test group, as measured by total score, apparently improved, to some degree, while the controls showed no significant change. These changes, which are of "suggestive" significance by our rather liberal criteria, might be of less than practical importance when compared with those for other populations. For example, when using a mean and a standard deviation derived from a group of mental hospital patients given by Lorr and associates,¶ one finds that the total score of our test group changes from 13.2 standard deviations above the mean to 11.4 standard deviations above the mean, a change which might be compared to a reduction of from 4+ to 3+

§ The standard formula for the *t* test involving correlated means, in small samples, was used for the comparison of those means which resulted from rating the same group on two different occasions. Where comparisons were made between the mean differences of the control group and the mean differences of the test group, the standard formula for the *t* test for uncorrelated means, in small samples, was used.

‖ Since, with small samples, it is extremely difficult to establish the two assumptions necessary for the *t* test, i.e., homogeneity of variance and normal distribution of the trait in the population, many statisticians recommend that a stringent level of significance, e.g., 0.01 and 0.001, be used in working with such samples. Because of this, we felt some misgivings in choosing the comparatively liberal levels of significance of 0.05 as "suggestive" and 0.01 as "conclusive" for the rejection of the null hypothesis of no difference. It was thought, however, that the consequences of rejecting a possibly useful drug might be more serious than would be an expenditure of additional time and money for further research should the results be equivocal.

¶ Lorr and others,[8] pp. 9, 16.

in the sugar content of a diabetic urinalysis.

The L-M Scale.—The difference in response as measured by midpoint ratings made on the test group and the midpoint ratings on the control group was of sufficient magnitude to reach the "suggestive" level of significance. The differences in response, as measured by the final ratings, were not significant. It is interesting to note that during the first half of the experimental period the behavior of the test group and that of the controls both worsened significantly, but to a greater degree in the controls than in the test group. Further, during the last half of the experiment, the period of increased dosage, the controls improved slightly but the test group remained unchanged. It would appear, then, that the drug had, in small doses, decreased the effect of unknown and deleterious factors which caused the worsening of behavior in the control group. It did not, however, in increased doses, maintain the advantage which the test group had gained over the controls.

Conclusions

It must be borne in mind that the drug was evaluated on the basis of minimal oral doses administered to chronic mental hospital patients. Considering these restrictions, we can hardly be enthusiastic in commenting upon the results. There has been no conclusive evidence of change in the patient's behavior as measured by the two rating techniques.

While somewhat less so than at the beginning, the patients remained very resistive, overactive, and, in general, poorly adjusted upon completion of treatment. This improvement is, therefore, negligible for practical purposes. Since the change from 2 to 4 mg. per day showed no practical effect, we cannot be impressed with the effect of doubling the initial dose.

On the basis of these observations we must conclude that reserpine given orally to chronic mental hospital patients has little or no measurable impact on behavior over a five-month period. We, therefore, cannot agree with certain other authors who suggest that a minimal dosage of reserpine can produce highly positive effects on such patients.

Summary

Fifty mental hospital patients were selected from a regressed ward for an "experimental-control" type study to evaluate the behavioral effects of oral dosage of reserpine (Serpasil, Ciba) over a five-month period.

Selection of patients was made on the basis of irascible ward behavior over a three-year period.

The experimental group was given 1 mg. of reserpine b. i. d. for a two-month period, followed by 2 mg. of reserpine b. i. d. for a three-month period. The control group was given placebo in identical quantity and frequency. Identification of the two groups was unknown to all persons involved in the study.

Patients were rated on two rating devices. One was used by ward personnel (registered nurses or psychiatric aides), and the other was used by two psychologists and a ward physician. Ratings of the experimental and control groups were compared on the basis of their performance before the study began, at the time of increase in dosage, and at the completion of the study.

Using currently accepted statistical techniques, improvement of "suggestive," but not "conclusive," significance was found in total behavioral adjustment, activity level, and compliance, as measured by the above-mentioned scales; however, the magnitude of these changes was negligible.

Reserpine was not demonstrated to be of practical value in the large-scale treatment of chronic, seriously regressed, overactive mental hospital patients.

St. Peter State Hospital.

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N-Methyl-a,a-Methylphenylsuccinimide in Psychomotor Epilepsy Therapy

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Introduction

In two previous reports * it was stated that in the course of investigation on the effect of N-methyl-α,α-methylphenylsuccinimide (PM 396) upon petit mal epilepsy, a favorable action of this drug was noted on the psychomotor element sometimes associated with petit mal attacks. Since to date psychomotor epilepsy is the most difficult of all forms of epilepsy to treat and there are no outstanding drugs in the therapeutic armamentarium for the treatment of this condition, this particular investigation was carried further. It is now possible to report results on 35 cases of psychomotor epilepsy treated with this drug.

Pharmacology

N-methyl-α,α-methylphenylsuccinimide (hereinafter designated by its laboratory number PM 396) was synthesized in the laboratories of Parke, Davis & Company. Figure 1 shows the chemical structure of N-methyl-α,α-methylphenylsuccinimide (PM 396; Celontin).

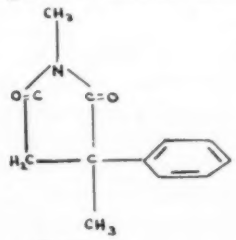

Figure 1

As was previously reported,[2] in the animal laboratory † a dose of 65 mg. of PM 396 per kilogram of body weight was effective in protecting rats against convulsions induced by pentylenetetrazol (Metrazol), as against a dose of 125 mg. of phensuximide PM 334 (Milontin) and a dose of 500 mg. of trimethadione (Tridione) per kilogram, suggesting an effectiveness, gram for gram, roughly twice that of PM 334 and eight times that of trimethadione. Biochemical, hematologic, and urinary findings remained within the normal range in animals given relatively large doses for prolonged periods of time.

Definition

The term psychomotor epilepsy is not a completely satisfactory term for describing seizures of the kind reported upon here. In its present usage it generally refers to that form of epilepsy characterized by automatic, stereotyped movements, which are reflections of disordered and confused psychic functioning. A wide range of behavioral manifestations is usually present, however, and the physician is faced with the difficult task of accurate clinical differentiation and diagnosis of the psychomotor type of seizure. As was mentioned above, the problem is often complicated further by the presence of petit mal and/or grand mal attacks in the same patient, along with psychomotor elements.

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From the Columbia University College of Physicians and Surgeons, and the Division of Child Neurology, the Neurological Institute of New York.

* References 1 and 2.

† Studies by Dr. Graham Chen, Parke, Davis & Company Laboratories.

Electroencephalography has contributed substantially to the clarification of definition in psychomotor epilepsy, and as Gibbs and Gibbs point out,[3] "continued studies have shown that psychomotor epilepsy is common, that it is usually associated with a focus of seizure activity in the anterior temporal area, and that this is by far the commonest type of cortical epileptic focus."

Gibbs and Gibbs also report that "the typical psychomotor focus is composed of random spikes, but focal grand mal, petit mal, and petit mal variant discharges are also encountered. No matter what the pattern," according to the Gibbses, "if the focus is in the anterior temporal area the clinical seizures are likely to be of the psychomotor type, manifesting complex, poorly coordinated movements, and confusional behavior. When the discharge is typical, the clinical seizure is typical. If the pattern is atypical—of the petit mal or grand mal types, for example—the clinical seizure is likely to be somewhat atypical, and to include features suggestive of petit mal or grand mal epilepsy."

While these electroencephalographic findings are helpful and constitute an important step forward in delineating psychomotor seizures from other forms of epileptic attacks electroencephalographers do concede that the correlation between EEG data and psychomotor attacks observed clinically is often very low. According to Gibbs and Gibbs,[3] "The view of psychomotor epilepsy obtainable from the waking electroencephalograms is inadequate, for waking records show seizure discharges in only 30 per cent of patients with a clinical history of psychomotor seizures, and the abnormalities which appear in the waking record are often not clearly focal. On the other hand, in 88 per cent of patients with clinical psychomotor seizures only, (i.e., with no other type of seizure) recordings made during sleep show focal seizure discharges in the anterior temporal region."

Selection of Cases

Cases in the present study were selected from patients with a clinical history of psychomotor seizures over a period of years. Table 1 shows the distribution of types of seizures in our series of cases, all of which have a psychomotor element.

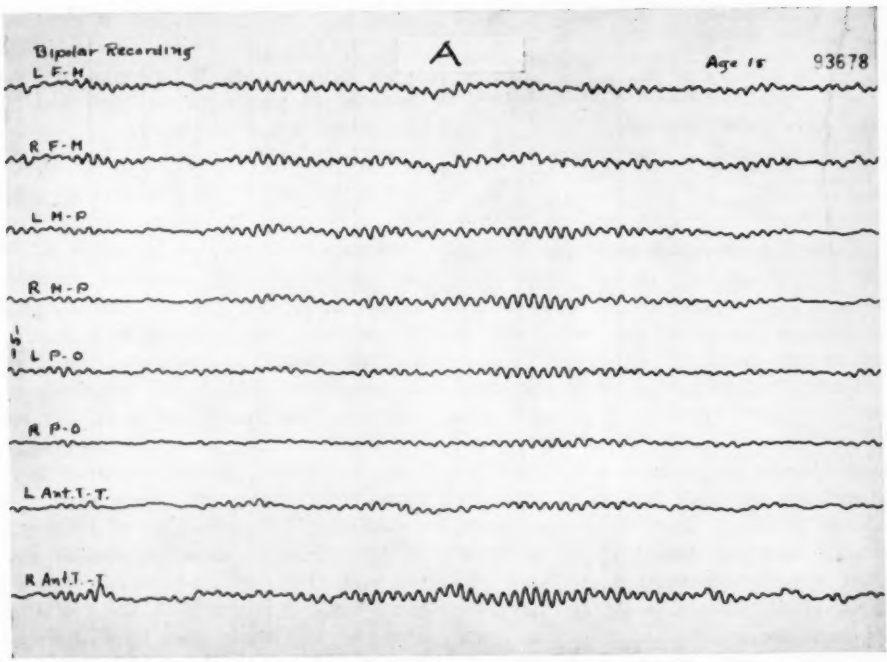
TABLE 1.—*Distribution of Seizures in Our Series of Patients with Psychomotor Seizures*

	Number	Per Cent
N = 35		
Psychomotor seizures only	9	25.5
Psychomotor seizures plus petit mal	6	17.0
Psychomotor seizures plus grand mal	16	46.0
Psychomotor seizures, grand mal and petit mal	4	11.5

It may be seen from Table 1 that in only 25.5%, or approximately one-quarter of the total case load, psychomotor seizures appeared alone. In three-quarters of the patients in the series, psychomotor seizures were combined with the petit mal and/or grand mal type of attacks.

EEG recordings were obtained from 31 patients in this series having psychomotor seizures. Samples of recordings from three of these patients at the beginning of treatment are given in Figure 2*A*, *B*, and *C*.

A, *B*, and *C* of Figure 2 show differences in EEG patterns of patients with a clinical diagnosis of psychomotor seizures. These tracings range from normal (*A*) to one in which an anterior temporal spike focus may be seen (*C*), the latter being suggestive of the psychomotor pattern of seizures when it appears in the EEG. The samples (Fig. 2*A*, *B*, and *C*) are characteristic of the EEG recordings which were obtained in the present study showing wide individual variation.


Bipolar Recording
A
Age 15
93678
L F-M
R F-M
L M-P
R M-P
L P-O
R P-O
L Ant.T.-T.
R Ant.T.-T.

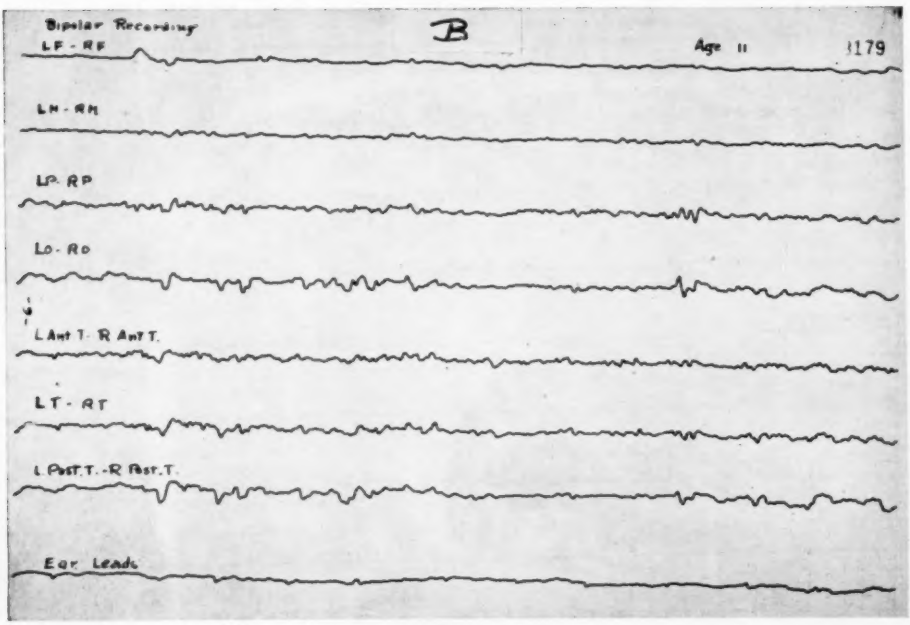

Bipolar Recording
B
Age 11
3179
LF - RF
LM - RM
LP - RP
LO - RO
L Ant T - R Ant T.
LT - RT
L Post.T. - R Post.T.
Ear Leads

Figure 2

TABLE 2.—*EEG Findings in Patients with Psychomotor Seizures Observed Clinically*

	Number	Per Cent
N — 31		
Suggested focus in anterior temporal lobe	2	6
Convulsive features	6	19
Generally abnormal—no specific features	20	65
Normal	3	10

Table 2 summarizes our EEG findings for the 31 patients in our series with clinical psychomotor seizures and EEG recordings taken at the beginning of treatment.

Table 2 indicates that the largest number of patients (20, or 65%), had EEG's which showed some abnormality, but that this was not peculiar to epilepsy. Six other cases (19%) had EEG tracings which revealed features often found among epileptic patients, but without more specific connotation. In only two cases (6%) were spiking and anterior temporal foci present, and in three cases (10%) the EEG recording was normal. It was necessary, therefore, to continue using an empirical method of classification for psychomotor epilepsy, based upon observation of seizures, as was done in the past with the petit mal and grand mal types of attacks.

We believe it should also be remembered that the EEG has certain limits of sensitivity. In the literature these limits are invariably presented in mathematical terms and therefore naturally foster statistical, but not physiological, reasoning. In our opinion, the anatomical and physiological bases for the limits of sensitivity of the EEG are really not generally visualized, and it is this lack of understanding that encourages the "specific area," or compartmentalized type of reasoning still so prevalent in medicine. The limitations of sensitivity of the EEG were demonstrated by Zimmerman and Putnam [4] in investigating the relation between EEG and histologic changes following the application of graded force to the cortex of the cat. In that study it was shown that within a

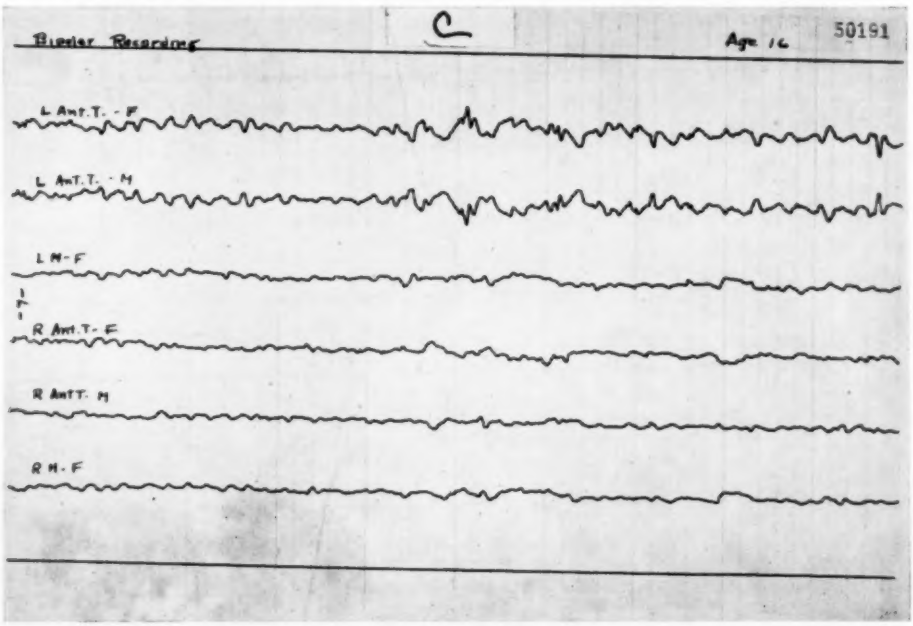


Figure 2 (Continued)

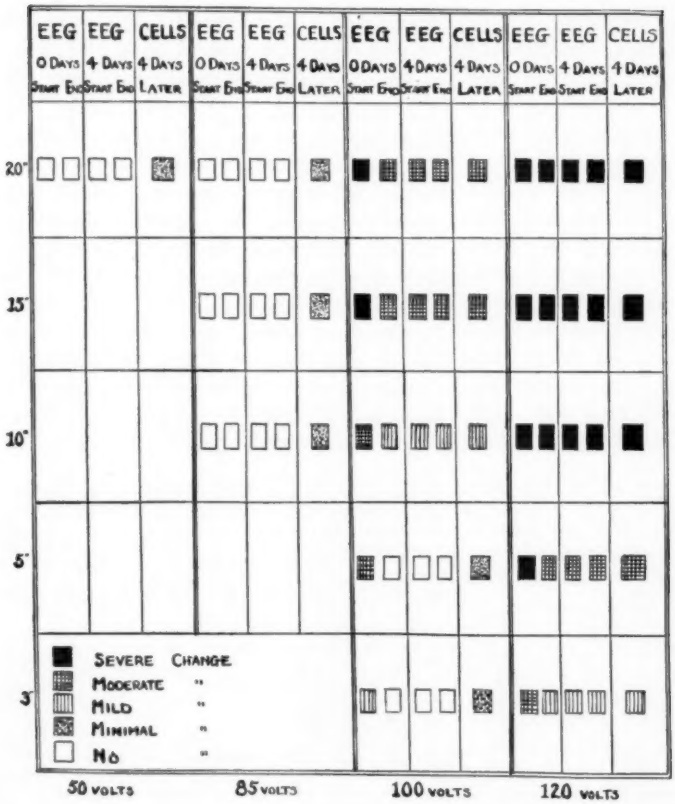


Fig. 3.—Degree of electroencephalographic change immediately after trauma, 45 minutes later, and 4 days later, and the degree of histologic change 4 days later, in relation to the intensity and duration of the force applied.

certain critical range cortical-cell change and EEG change varied directly with the amount of force applied to the cortex. Below that critical range, however, cortical-cell change was still seen, but with a normal EEG. Figure 3 illustrates these findings graphically.[4]

It may be seen from Figure 3 that the most pronounced electroencephalographic and histologic changes resulted from the application of a force equivalent to 120 volts within a time range of 10 to 20 seconds. When a force of 50 volts was applied for 20 seconds, minimal cell changes were still present, but EEG tracings were normal.

In our opinion, the preceding data reemphasize the important point that, just as one can have cortical-cell change with a normal electroencephalogram following trauma, so one can have a normal electroencephalogram in the presence of psychomotor epilepsy, or any type of epilepsy. Therefore one should not use the EEG alone as the crucial diagnostic tool.

Results

The choice of base line is of great importance in estimating the effectiveness of anticonvulsant medication, as was reported previously.[2] This is because interpretation of results depends upon the initial criterion used in evaluating degree of reduction in, or control of, seizures following the administration of any drug.

In the present study we used the drug immediately preceding PM 396 as a base

line for testing the effectiveness of the latter on psychomotor seizures. Since it has been our experience that seizures are generally reduced over a period of time regardless of the particular type of medication given, by the use of so recent a criterion, rather than a base line more remote in time, data are subjected to the most rigid interpretation possible. Findings reported herein therefore, we believe, are very conservative.

Table 3 shows results obtained with PM 396 in the treatment of psychomotor epilepsy when the drug immediately preceding PM 396 is used as a base line for comparison of effectiveness.

TABLE 3.—*Effectiveness of PM 396 in Controlling Psychomotor Seizures Using the Drug Immediately Preceding PM 396 as a Criterion of Comparison*

N = 35	
Average no. of seizures per week previous drug	7
Average no. of seizures per week on PM 396	3
Reduction in seizures	57%
Average daily dose, gm.	1.2
Average duration of treatment, wk.	19
Complete control	20%
Practical control (80%-99%)	17%
Partial control (5%-79%)	37%
No effect (0-4%)	26%
Worse	0%
Toxic	14%

Complete control (absence of seizures for at least four consecutive weeks) was reached by 20% of the cases (Table 3); practical control (80%-99% reduction in seizures, by 17%, and partial control (5%-79% reduction in seizures), in 37%. This makes a total of 74%, or approximately three-quarters of the patients, receiving some benefit from PM 396 in classification had a reduction in seizures, and leaves 26%, or about one-fourth of the cases, unaffected.

If the category of partial control, which is very wide, is considered, results show that 78% of the cases in this classification had a reduction in seizures of at least 50%, and 22% of the patients, a reduction below 50% of the former rate. This means that of the entire case load, 66%, or two-thirds of the patients with psychomotor seizures, had a reduction of at least 50% beyond that of the previously administered drug at the end of the treatment period with PM 396.

As was mentioned previously, PM 396 was investigated originally as a petit mal drug and subsequently demonstrated effectiveness in the treatment of psychomotor attacks. In dealing with the drug over a period of years, the impression emerged clinically that some benefit appeared to be derived from the addition of PM 396 to standard anticonvulsant medication in the treatment of grand mal seizures, in cases having petit mal and grand mal combined. It was therefore decided to investigate data from a statistical standpoint in order to verify this clinical impression. Table 4

TABLE 4.—*Effect of PM 396 added to standar anticonvulsants in controlling grand mal seizures in patients having a combination of grand mal and petit mal, using the drug immediately preceding PM 396 as a criterion of comparison*

N—31	
Average no. of seizures per week previous drug	3
Average no. of seizures per week on PM 396	2
Reduction in seizures	33%
Average daily dose, gm.	1.2
Average duration of treatment, wk.	30
Complete control, %	35%
Practical control (80%-99%)	3.5%
Partial control (5%-79%)	26%
No effect (0-4%)	32%
Worse	3.5%
Toxic	6%

gives the results obtained after PM 396 had been added to standard anticonvulsants in the treatment of grand mal seizures which appeared along with petit mal in the same patients.

Complete control was reached by 35% of the group (Table 4) and practical control by 3.5%, while 26% of the group fell into the category of partial control of seizures following treatment. This makes a total of 64.5% of the group receiving some benefit following therapy, over previously administered drugs. Although the group is small, results seem to indicate that PM 396 may prove a valuable adjunct to standard anticonvulsant medication for the control of the grand mal type of seizure, at least in patients having a combination of petit mal and grand mal attacks.

Dosage

The average dose in our series of patients with psychomotor seizures was 1.2 gm. per day. This was administered in units of 0.3 gm. capsules, or an average of 4 capsules per day. The range of effective dosage varied, however, from 0.3 to 2.4 gm. per day, or from 1 to 8 capsules per day. The usual procedure of administration was to give 0.3 gm. each week if attacks were not controlled and toxic side-reactions did not develop, until the average of 4 capsules per day was reached. When toxic signs appeared, they could usually be controlled by reducing the dose to a lower level, or by discontinuing the drug entirely and then working up more slowly to the optimal dose.

TABLE 5.—*Toxic Signs Appearing in Our Series of Patients with Psychomotor Seizures While on PM 396*

N = 5	
Fatigue, listlessness, drowsiness	2
Loss of appetite	2
Rash on face and chest	1
Dizziness	1
Weight loss	1
Periorbital edema	1
Pallor	1

Toxic Signs

Toxic signs appeared in five patients, or in 14% of our group having psychomotor seizures, while under medication with PM 396. The nature and incidence of these toxic side-effects are given in Table 5.

Table 5 shows that the number of toxic side-effects encountered with PM 396 is greater than that reported for phensuximide (Milontin).[1] They are not serious, however; and the good therapeutic results obtained, we believe, justify the use of PM 396 in patients with psychomotor seizures.

No blood dyscrasias have been observed over a three-year period of study; nor have pathologic changes in the urine have been observed so far.

Summary

To date psychomotor epilepsy is the most difficult of all forms of epilepsy to treat, and there are no outstanding drugs in our therapeutic armamentarium for the treatment of this condition. N - methyl - α,α-methylphenylsuccinimide (PM 396) has been found to be an effective drug in the treatment of psychomotor epilepsy.

Seventy-four per cent of the patients treated showed a reduction in psychomotor seizures following treatment with PM 396, and 66%, a reduction of at least 50% beyond that of the previously administered drug at the end of the treatment period.

Furthermore, the drug is not seriously toxic to date, and no blood dyscrasias have been observed.

11 E. 68th St. (21).

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Case Reports

"PHANTOM" SCIATICA

ARTHUR B. KING, M.D., Sayre, Pa.

PAIN COURSING along the distribution of the sciatic nerve is a common symptom of compression of one or more of its roots. Protruding intervertebral discs are by far the commonest producers of sciatica, and this disorder is being recognized with increasing frequency. The distribution of pain following root compression in patients in whom part of the peripheral portion of the sciatic nerve is missing proved of sufficient interest to warrant notation.

During recent years two patients have come under observation who have sustained a protrusion of an intervertebral disc and who had, in addition, sustained a major amputation of a lower extremity before the onset of back complaints. Both were active men of middle years, well adjusted to their deformities, neither of whom had had any previous complaints that might have suggested phantom limb phenomena.

Report of Cases

CASE 1.—The patient was a large, muscular machinist, 49 years of age, when he entered the Robert Packer Hospital in June, 1951, with the complaint of severe back pain and sciatica in the left leg. The left leg had been amputated about 4 in. below the knee following an industrial accident in 1948 during which the foot and ankle had been extensively crushed. Convalescence had been rapid, and there had never been any complaints referable to the leg. A prosthesis was habitually used, and the absence of the lower portion of the extremity did not interfere with the patient's work as a machinist or his daily routine.

In March, 1951, the patient had slipped off a wagon and twisted his back. The lower back remained "sore," and that night he was awakened by a "sharp" pain in the left buttock. The discomfort persisted, with fluctuations in intensity, until four weeks later, when he experienced a full-blown sciatica. The pain radiated from the lower back, across the sacroiliac region, through the buttock, down the posterior thigh to the knee, across the lateral aspect of the lower leg, across the dorsum of the absent foot and into the great and second toes, which were not there. The discomfort was sharply and accurately described. The patient insisted he "knew" where the pain was, despite the fact that he was fully aware that the lower leg and foot had long been absent. The spatial location of the pain was precise and left no doubt in his mind. Furthermore, he stated he had never experienced anything like it before. The discomfort was aggravated by coughing, sneezing, walking, laughing, and bending.

The usual clinical findings of a protruding disc were present. The straight-leg-raising test was positive on the left at 70 degrees, there being an exaggeration of the pain in the absent ankle and foot. The left knee jerk was present. No sensory deficits could be demonstrated in the remaining portion of the left lower limb. Subsequent myelography indicated a protruding intervertebral disc at the L 4-L 5 interspace, which was removed at operation the following day.

Convalescence following surgery was rapid. The pain in the left leg was completely relieved by the third postoperative day. Over the succeeding years there have been episodic "backaches." The only complaint referable to the left leg has been transitory "tingling" of the absent toes.

CASE 2.—A 57-year-old laborer first entered the Robert Packer Hospital in January, 1954, with the complaints of backache and pain in the right leg. During World War I he had received a machine-gun wound of the left lower leg. This was followed by gangrene, resulting in an amputation through the lower third of the femur. A prosthesis had been worn since recovery. The patient earned a living as a utility man in a glass factory, and the loss of the left lower limb was in no way disturbing.

About two months before he was first seen he had noted low backache. Shortly after this, while lifting a bucket of cullet, he felt something "snap" in the low back. This sensation was immediately followed by severe low-back pain and right-sided sciatica. Conservative measures failed. Myelography demonstrated a defect at the L 4-L 5 interspace, and a protruding intervertebral disc at this

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level was removed. Initially, convalescence was satisfactory, but three months postoperatively, during a violent spell of coughing, the patient had a recurrence of back pain and right sciatica. Symptoms were pronounced, and again conservative measures failed. Reexploration of the L 4 interspace was undertaken, and it was discovered that an additional piece of disc material had been extruded. Following removal, the symptoms were relieved, and the patient returned to his usual occupation.

In October, 1946, while rising from a sitting position, he again had a sudden excruciating pain in the low back and almost immediately developed left-sided sciatica. The patient remarked that "the pain shot out of my back, down my butt, out of the stump and into my big toe that hadn't been there for years." This man had never had any symptoms suggestive of causalgia or phantom limb. The stump was not troublesome, and he states that he had not thought about the foot for years.

Symptomatic treatment had been carried out by his local physician, without benefit. When seen two weeks later, the patient was most uncomfortable. The paravertebral muscles were in pronounced spasm, and there were no voluntary back movements. Pressure over the L 4 and L 5 spinous processes was painful and produced "electric shocks" down the left leg. The stump could be elevated only 30 degrees off the bed. The leg having been amputated at the midthigh precluded the possibility of testing motor power, reflexes, and sensory deficits in the lower leg. However, the patient had no difficulty in precisely relating the pain distribution over the L 5 dermatome, even though this portion of his anatomy had been removed some 27 years before.

The usual disc approach on the left was carried out, and, to our surprise, another huge piece of cartilage had extruded out of the L 4 interspace. All the sciatica had disappeared by the end of 48 hours, and the back felt well enough that he got out of bed, put on his artificial leg, and walked down the hospital corridor at the end of 72 hours. He has had no complaints for the last year and is now well and working full time.

Comment

When adequate irritation is applied to one of the sciatic roots, even the unintelligent patient will adequately delineate the area of his referred pain. At times the pain seems projected beyond the toes or heel for an indefinite distance in space outside of the foot. I have had many patients tell me that the pain "shoots down the leg, across the foot, into the toes, and right on out." The special pattern is very well fixed in the brain and certainly appears to persist precisely long after the peripheral nerves have disappeared.

The nature and explanation of phantom limb pain and causalgia are still far from clear. It is my impression that the difficulties reside in the higher cortical levels, although I am aware that this will be violently disputed by some. My own experience would lead me to believe that ordinary stable persons do not develop these things following amputation. Most people will relate, however, when specifically questioned, that they can "feel" the missing part and may be able to "wiggle it," but that none of this is troublesome and must be actively recalled to the sphere of consciousness.

The experiences in the two cases related above indicate that the sensory roots of the amputated nerve can be stimulated in the ordinary manner and that a typical radiation of pain is produced. Likewise, it follows the usual course in that when the irritation is removed, the pain promptly subsides. Even though the pain was present for some weeks, it remained exactly the same and was in no way different from that experienced by a person whose anatomy is intact. Neither patient complained of anything that resembles the syndromes of phantom limb and causalgia, either before or after operation. It might also be remarked that both patients were industrial liability cases and that both requested permission to return to work before the end of the usual convalescent period.

Often when protruding discs compress the root severely, or the roots are unduly stretched at operation, permanent injury to some of the sensory components ensues, resulting in the complaint of "numbness." Neither of the patients under discussion had any "phantom numbness" after operation. Lack of sufficient injury to the roots, rather than the ability to appreciate the feeling, would seem to account for its absence.

What part retrograde degeneration of a nerve plays in the physiologic functioning of the spinal root and central nervous system, I do not know. In at least one case, 27 years after amputation of a lower limb in the midthigh region, spinal roots of the sciatic nerve and the L 5 root seemed to be functioning normally. Also, the presence of an amputation neuroma on the distal portion of the nerve in no way confused the expected radiation of pain originating at the L 5 root. There was no difficulty in the minds of the patients described as to just where their pain was. It was precisely described as to type, location, duration, and what aggravated or relieved it. When it was relieved, they were very grateful; in fact, one man remarked that he was "damned glad to get rid of that foot for the second time."

The absence of the legs did not delay arrival at the correct diagnosis. It merely removed some of the confirming physical findings that comfort the physician when present and leave him uncertain when absent.

Summary

Two patients who sustained protruding intervertebral discs with sciatica in previously amputated legs are described. The distribution of pain was characteristic of a single-root irritation, the partial absence of the affected extremity notwithstanding. Both were promptly relieved by removal of the offending disc. At no time was there anything to suggest causalgia or "phantom limb pain."

Books

Grosse Nerven Aerzte: 21 Lebensbilder. Edited by Kurt von Kolle. Price, 29.4 D.M. ($7.00). Pp. 294. Georg Thieme Verlag, Herdweg 63, (14a) Stuttgart N (American Zone), 1956.

This book contains rather complete biographical sketches of 21 "nerve doctors." It is heavily weighted with psychiatrists—there are 11 of them—this is not surprising, since the editor is a psychiatrist who heads the clinic that was formerly Kraepelin's. Besides the psychiatrists, there are four clinical neurologists, three neurosurgeons, and three nonclinical laboratory men.

Again, as one would expect, most of the great doctors are Germans (Berger, Bonhoeffer, Erb, Foerster, Griesinger, Gudden, Jaspers, Kraepelin, and Rieger); two, Austrians (Freud and Wagner-Jauregg); two, Swiss (Bleuler and Jung); two, English (Jackson and Sherrington); two, French (Charcot and Pinel), and one each, American (Cushing), Spanish (Ramón y Cajal), Portuguese (Egas Moniz), and Russian (Pavlov).

Most of the sketches have been written by men who were assistants to those of whom they wrote and others by medical historians. The results are very good but a bit irregular in excellence. Most of the articles tell of the work and interests of the biographers, and many of them tell much more about what kind of people they were. Considerable hero worship could not be kept out, but on the whole the stories are factual and conservative. In the note on Pinel the author goes at considerable length into the subject of psychiatry at the time of Pinel and makes an interesting story of it. Incidentally, John Fulton did Cushing and Sherrington and did them well. There is an appendix listing the neurological, psychiatric, neuropathological, and neurosurgical institutes and laboratories of the German-speaking countries, including lists of the names of those who have headed them, together with their dates.

On the whole this is an interesting book and well worth the time of anyone who wants to know about those masters. For any such it is a valuable contribution.

Le Systeme Nerveux Peripherique. By Guy Lazorthes, Professeur d'Anatomie à la Faculté de Médecine de Toulouse, Neurochirurgien des Hôpitaux, Doctor des Sciences Naturelles. Price, 4,200 fr. Pp. 348, with 214 illustrations. Masson & Cie, 120 Boulevard Saint-Germain, Paris 6e, 1955.

This book is an orderly arrangement of the anatomy of the cranial and spinal nerves, supplemented by brief summaries of their physiological functions and certain clinical applications.

In the first part of the book a chapter is given to a description of each of the cranial nerves. The second part includes individual chapters for spinal nerves, the major plexuses, and the principal nerves of thé extremities.

The emphasis is on anatomy, and the most attractive features of the book are the numerous labeled illustrations, of which there are 214 original line drawings. Many of these drawings are not just reproductions of anatomical arrangements, but diagrams which emphasize the relation of the nerve to other structures in various portions of its extent, from origin to ending.

The major essentials of the embryology, gross structure, vascularization, and important anatomical relationships of the nerves are here. Allusions to clinical applications in diagnosis of diseases of the nerves and in the application of surgery are meager, but they are ample enough to show the medical student the basis for diagnosis and treatment. Even the specialist in diagnosis and surgery of the nervous system will find ready access to anatomical details not often encountered in other texts.

Though the book is in French, the organization of the text, with appropriate captions to sections and short, concise paragraphs, makes easy and pleasant reading, even for those less versed in the French language.

Section on PSYCHIATRY

Janet and Freud

PERCIVAL BAILEY, M.D., Chicago

"And now from the Vast of the Lord will the waters of sleep
Roll in on the souls of men
But who will reveal to our waking ken
The forms that swim and the shapes that creep
Under the waters of sleep?"

SIDNEY LANIER

In the textbooks of psychiatry nowadays, Pierre Janet is dismissed in a few brief remarks as one who just failed to realize the beginning of the millenium. This estimate I believe to be unjust, and I take this opportunity to discuss with you a few of the erroneous statements which are made concerning his work in its relation to that of Sigmund Freud, since I have doubtless read more of Janet's work and know more about him than anyone else in this audience.

The neglect of Janet's work seems to me to arise from several sources: 1. From ignorance. Few American psychiatrists any longer read French, and most of Janet's work has never been translated. 2. Psychiatry has recently been unduly influenced by men and women born in Germany and Austria; they know the German literature best and naturally stress it. 3. Most of these men were pupils of Freud or his discipiles and jealously warded off any threat of his system. But more important, I believe, is another reason. 4. The two men represent two traditionally opposed ways of looking at man and his relation to the universe. I shall hope to develop this theme.

Now let us look at a few of the erroneous statements which have been made of Janet's work in its relationship to Freud's. I must suppose that you are familiar with the main outlines of the work of both men, an unjustifiable supposition in the case of Janet, but time does not permit me to proceed otherwise. For the same reason I shall be obliged to make rather dogmatic statements, but I assure you that I have in my desk a version thrice as long, with chapter and verse for every statement and much more besides.

(1) *Janet Was Hostile to Freud.*—We might as well get this one out of the way in the beginning, since there is not an iota of evidence to support it, unless one takes the attitude that he who is not one hundred per cent for us is against us. I have often heard Janet discuss Freud's work, and never did I detect any trace of hostility. In 1913, in his discussion of psychoanalysis before the International Congress of Internal Medicine at London, Janet wrote: "Beneath the exaggerations and the illusions which disfigure psychoanalysis, are found a great number of precious studies on the psychoneuroses, on the evolution of thought in infancy, on the divers forms of sexual sentiments. These studies have drawn attention to little known facts which, because of a traditional reserve, one was disposed to neglect. Later one will forget the strained exaggerations and the adventurous symbolisms which today seem to characterize

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Summary of an already much-abbreviated essay read to the Illinois Psychiatric Society as a Presidential Address, May 18, 1955.

these studies and distinguish them from scientific works and will remember only one fact, that psychoanalysis has rendered great service to psychological analysis." And just a few months before his death he remarked to my friend Henri Baruk that his attention was fixed on the general and impersonal mechanisms of the spirit, whereas Freud's was fixed on the subjective personal foundations of each individual.

(2) *Janet Was a Predecessor of Freud.*—Freud began where Janet left off. On the contrary, Freud was the elder, being born in 1856, while Janet was born in 1859. The two were contemporaries, each elaborating his system largely in isolation from the other, and Janet survived Freud by eight years, dying in 1947, at the ripe age of 87. He continued to publish illuminating studies of abnormal psychology until the very year of his death.

If the statement be understood to mean that Janet was a stimulus to Freud in his work, then there is some truth in the statement but not much, although we know, from his letters to Fliess, how apprehensive Freud was when a new book by Janet was published. Freud is often said to have come under the influence of Janet at the Salpêtrière. This is not true. Freud was at the Salpêtrière from Oct. 13, 1885, to Feb. 28, 1886. During this period Janet was teaching philosophy in the Lycée at Le Havre. He did not come to Paris until the autumn of 1889, when he returned to medical school and was invited by Charcot to open a psychological laboratory in his clinic. Both Freud and Janet were greatly influenced by Charcot; each published his first psychopathologic study in 1886, Freud's dealing with male hysteria, a subject on which Charcot had lectured in the winter semester of 1885-1886. In the same year Dejerine published his first psychosomatic study. In 1884, Hack Tuke had published his "Effect of the Mind on the Body." The time was ripe for psychogenesis. It was in the air.

There is some evidence of an early influence of Janet on Freud, however. In 1909, Freud was invited to give lectures at Clark University. In one of them he stated that he followed Janet's example when he made mental splitting and the dissociation of personality the central points of his theory. Later on, in his autobiography, he denied this in a curt passage, writing that historically psychoanalysis was completely independent of Janet's discoveries. After that no disciple of Freud would bother to read Janet. Why did Freud make this statement? Had he forgotten? If so, we must suppose that it was one of those motivated forgettings which he had so abundantly elucidated in his patients. This is entirely possible, since we know that Freud was an excellent forgetter. But why did he forget his debt to Janet and readily admit his debt to Charcot and Bernheim? The motivation is not difficult to find. Charcot and Bernheim were dead, and Janet was very much alive, a powerful rival, and we know that Freud could never brook a rival. We know from his letters to Fliess with what anxiety he scanned the writings of Janet. Moreover, Janet had published a critique of psychoanalysis in 1914, not unkind, but shrewd and logical, in which he pointed out some of the defects of the psychoanalytical method which were becoming all too obvious. One of the defects pointed out by Janet was the unreliability of the statements made by neurotic patients, which Freud had already found out; furthermore, he pointed out how easily the auditor distorted what he heard so that he (Janet) early adopted the practise of making notes constantly during his interviews. The realization that the very method by which he collected his data contained a fatal flaw drove Freud almost to collapse, as is evident in his letters to Fliess. During this period he suffered from a "very considerable psychoneurosis" and thought seriously of giving up his studies of psychopathology. Why did he go on? In 1914 Freud wrote that perhaps he persevered only because he had no choice and could then begin again at anything else, adding that at last came the reflection, etc., etc.—so begun the ratiocination. One is reminded

of Tertullian's defiant cry: *"Credo quia ineptum."*

Nuttin says that the theory of Janet regarding the split personality lies at the root of the Freudian idea of the two zones of psychic life, the conscious and the unconscious. Ah, yes. But was the idea Janet's? It is true that Janet had developed the idea in his lectures at Harvard in 1906, about all of Janet that most psychiatrists have ever read. But the idea is far, far older than that. Maybe Freud got it from Janet, but he did not need to. It was at least as old as Leibniz and was in the air when Janet and Freud both were students. Brentano — Freud's teacher—traces the concept back to St. Thomas Aquinas. This has been pointed out so often that I would not mention it except that it gives me a chance to quote two remarkeable Americans. On June 29, 1870, in a memorable address delivered before the Phi Beta Kappa Society at Harvard University, Oliver Wendell Holmes remarked that it is a great source of error to suppose that there is no perception in the mind but that of which it is conscious. And William James, in his Gifford Lectures, delivered in Edinburgh in 1901, stated that he could not but think that the most important step forward that had occurred in psychology since he had been a student of that science was the discovery, first made in 1886, that, in certain subjects at least, there is not only the consciousness of the ordinary field, with its usual center and margin, but an addition thereto in the shape of a set of memories, thoughts, and feelings which are extramarginal and outside the primary consciousness altogether but yet must be classed as conscious facts of some sort, able to reveal their presence by unmistakable signs. To whom does he attribute this important step? To Janet? To Freud? No, since in that year each of them published his first psychopathological study and in neither of them is this concept developed. He attributes it to a Mr. Myers. What of it? The concept was known long before Janet, Freud, or Myers. Yes, you will say, but Freud first showed that elements present latently or unconsciously in the psyche do not necessarily remain in a state of impotence and inactivity. Listen again to Oliver Wendell Holmes.

"There are thoughts that never emerge into consciousness, which yet make their influence felt among the perceptible mental currents, just as the unseen planets sway the movements of those which are watched and mapped by the astronomer. Old prejudices, that are ashamed to confess themselves nudge our talking thought to utter their magisterial veto. . . . We know very little of the contents of our minds until some sudden jar brings them to light, as an earthquake that shakes down a miser's house brings out the old stockings full of gold, and all the hoards that have been hidden away in holes and crannies." Did Freud ever express it better?

Now, I am quite convinced that Janet did not get the idea from Holmes, and Holmes says he got it from Lecky. There were other sources available to Janet, who probably never read either Holmes or Lecky, and there were plenty of German sources available to Freud aside from Leibniz. Although Freud began his psychological studies in blissful ignorance of much of the work of his predecessors and always remained an amateur philosopher, we do know that he followed the seminars of Brentano, the theoretician of empirical psychology in Vienna, and Brentano was a former priest. But he later read very little because, as he wrote to Fliess, he found his own ideas expressed better than he could express them and it robbed him of the thrill of discovery (Letters 29 and 95). It is exceedingly difficult to have an entirely original thought.

Freud has been accused of getting the idea of the influence of traumatic experiences from Janet. It is true, that in his thesis on psychological automatism, Janet mentioned histories of such experiences, even a beautiful example of recovery after catharsis, but this thesis was published in 1889, five years after Freud was in Paris, and he first used the concept in his writings in 1886.

Strangely, Janet, who reported many instances in his studies of neuroses and fixed ideas (1898), has been accused of getting the idea from Freud by Madeleine Cavé. The truth of the matter is that they both got it from Charcot, who expounded the idea in a lecture delivered on the first of May, 1885, just before Freud arrived in Paris. This lecture was translated by Freud and sent to the publisher in December, 1885. The translation was published in German before the French appeared, a fact of which Freud was very proud. This is the way Charcot presented the matter, and he says he got it from a Dr. Reynolds.

"Now, by reason of the obnubilation of the Ego produced in one case by hypnotism; in another case, as we have imagined, by the nervous shock, this idea once installed, fixed in the mind and reigning alone, without control, would be developed there and acquire enough force to manifest istself objectively in the form of paralysis."

But enough of questions of priority. After long and laborious study it is my conviction that Freud and Janet influenced each other very little. If they often come to similar conclusions that is not remarkable. The history of science is full of such instances where several investigators in widely separated parts of the world have arrived at the same solution of a problem simultaneously and independently. In the present instance others than Freud and Janet and Charcot were familiar with the continued influence of traumatic experience. It is usually wrong to speak of dishonesty in a case where an author fails to mention the work of a predecessor. Listen again to that wise American, Oliver Wendell Holmes. "Honest thinkers are always stealing unconsciously from each other. Our minds are full of waifs and strays which we think are our own. Innocent plagiarism turns up everywhere." This essay is filled with such "waifs and strays." Since I disclaim any originality for anything in it, except the arrangement of the material, I dispense with citation of authorities except when they come readily to my remembrance.

Recently Jones has published what he calls a formidable list of fifteen of the leading ideas which have been supposed to be original with Freud that are to be found in the writings of his predecessors or contemporaries and with which Freud was thoroughly familiar. The most that any of us can hope to do, Freud and Janet included, is to present an idea a little more clearly, or from a viewpoint different from that of our predecessors. No one can accuse Freud of not presenting his views in a novel way; or Janet either. Whenever anyone presents a matter in such a way, the first reaction of his contemporaries is a shocked rejection. After a while they begin to say that, after all, it was well known before. Finally they attempt to incorporate it into their own systems. And in all of these reactions there is much truth. One is struck first by the new aspect of the old truth which becomes apparent only after the original shock has worn away and experience has corrected the exaggeration of the new viewpoint. It is then possible to incorporate the partial truth into any related system.

This process was far more obvious in the case of Freud because of his inveterate habit of generalizing from single cases, often himself, which led him often into error and caused him much heartache. A good example is the matter of incestual trauma in infancy. When Freud first presented this theory at a meeting of the Viennese Medical Society, Krafft-Ebing remarked that it sounded to him like a scientific fary tale. This remark hurt Freud deeply, but he had to admit later that this was the exact truth, and the realization threw him into a severe depression, as he tells in his letters to Fliess. Janet, a doctor of philosophy from the Sorbonne, never fell into such a trap. This Naïveté of Freud was one of his defects, and there is nothing to gain by trying to hide the fact. I think this is the place to insert the warning written in 1941 by Roy R. Grinker, the Director of the Institute for Psychosomatic and Psychiatric Training and Research. "Psychoanalytic science will

be much more progressive and productive, in the way Freud himself would have wished it to be, if we do not deify him and deny him the human privilege of error."

(3) *Janet Was Superseded by Freud.*—Galdston has noted that the young psychiatrists seem to labor in the belief that before Freud there was little or nothing worthy of the name psychiatry; that all antecedent psychiatric history was but the forerunner to the fulfillment achieved in Freud and analysis. After ten years of examining for the American Board of Psychiatry and Neurology, I might add that they seem to me to have the same belief about contemporary psychiatry. This is the converse of the preceding statement, that Janet was a precursor of Freud. It is true that Janet's star paled as Freud's rose, but there are many signs of the development of a more equitable estimate of the two men.

One of the elements bringing this about is the realization of many older analysts that much of Freud's formulation must be revised. In France, Lacan has revised his ideas about early infantile eroticism. I do not need to tell this audience that the Chicago school has taken an active part in this reformation, taking into account more fully the hereditary, constitutional, social, educational, and biological factors whose neglect in his own writings Freud excused on the ground that others talked of them enough. To give a specific example, the important question why, with similar past history and subjected to the same strain, one person breaks and another not, the very basis of Janet's system of force, weakness, and tension, Freud consistently neglects. Eysenck interprets this neglect by saying that Freud was interested in understanding, not in explaining. Recently Edouardo Weiss, in a discussion of "Ego Strength and Ego Weakness," at the Veterans Administration Hospital in Palo Alto, said that we have to consider the psychic forces quantitatively and in terms of their distribution. In other words, we have to introduce a dynamic-economic point of view. This is pure Janet; he worked for nearly half a century to establish such a theory. The idea comes straight down in the French tradition from Jouffroy, in 1828.

Janet is a largely unexplored and unexploited mine from which numerous psychiatrists have rediscovered and will rediscover the most startling ideas and become famous by translating them into the analytical terminology. The process is an old one. We should not forget that Freud said that he made Janet's mental splitting and the dissociation of personality the central points of his theory. Also, Bleuler, in his great book on schizophrenia, says that the word *autismus* is only the positive facet of what Janet called loss of the sense of reality. The debt of Adolf Meyer to Janet is very great. I might quote also Adler's statement that Janet's emphasis on the neurotic's sentiment of incompleteness particularly was so wholly in harmony with the results offered by him that he was justified in seeing in his work an extension of that most important fundamental fact of the mental life of the neurotic. At this point I might point out that Adler's disciples are not immune to the temptation to elevate their master at Janet's expense. Way has written, "Neurosis, then, as Adler had found, and as Janet had confirmed, was a disease originating in function and bearing back upon function." This is just the reverse of his master's statement.

The process still goes on; the general point of view of King's recent monograph on the "Psychomotor Aspects of Mental Disease," that the basic adaptation achieved by means of the motor system in animals is one of the essential life processes, the greater control of which gives rise to mentation in animals and mind in man, is the very basis of Janet's psychology of conduct.

This great attempt of Janet to build a psychology of conduct is almost unknown in this country. It is rejected by the analytical school as too intellectual and ignored or relegated to a secondary place behind the predominance of conflictual tensions and their expression in complexes symbolized

in the symptoms. Yet it is necessary to the comprehension of the neurotic patient, and lately the analytical school has been obliged to resusciate these conceptions and translate them into its own terminolagy. The role of the terrain is being rehabilitated by giving back to the ego all its functional value. A very judicious estimate of these studies of Janet is given recently by Pierre Male, a member of the psychoanalytical institute of Paris, presided over by Marie Bonaparte. This is quite in line with the statement of Freud that psychoanalysis is able to give only partial explanations and needs to be completed by a psychology of the ego; also that the soft, insistent voice of the intellect will, in the end, make itself heard above the instincts.

Far from ceasing to work when Freud became renowned, Janet continued to develop very illuminating studies of abnormal psychology, which complement Freud's system in exactly the way Freud said was needed. His great synthesis of the psychasthenic syndrome is still valid and useful, if we cease to be preoccupied with the sense of individual symptoms. His works could profitably be studied by any psychiatrist, but, unfortunately, many are not translated into English. Recently Leonard Schwartz has published a summary of them in German, but it is dull reading, entirely lacking in the scintillating charm of Jante's witty intellect. They are, nevertheless, known to the French psychoanalysts and appreciated by them.

Paulus recently wrote: "We have the feeling that his first memorable discovery (splitting of the personality) will pale before the theory of the middle functions of the spirit, with which he closes his work, one of the glories of French science." Unfortunately the Second World War made it impossible for him to develop this theory systematically in a book on which he was working, and we have only stenographic copies of his lectures at the Collège de France, untranslated into English, of which I possess a complete set. They will be slowly incorporated into dynamic psychology, probably through the French group, because they furnish the necessary complement to the Freudian system.

(4) *Janet's Work Is Purely Descriptive.*—This feeling comes largely from the fact that most American psychiatrists have read nothing of Janet except the "Major Symptoms of Hysteria." But this was avowedly only a description of symptoms. Year after year at the Collège de France Janet exposed a dynamic psychology, starting from sources within the French tradition and using very little outside it. I say a dynamic psychology, although I am aware that recently the five eminent psychiatrists appointed by GAP to draw up a definition were unable to agree. Historically a dynamic psychology has been one which makes use of concepts drawn from 19th century physics, such as energy, inertia, tension, force, etc. In this sense, I know of three major dynamic systems of that type—those of Janet, Freud, and Jackson. For my present purpose recent formulations are irrelevant.

Just now the French psychiatrists are busy trying to make a synthesis of these three systems. Henri Ey is a good example of these psychiatrists. Why are they suddenly occupied with this task and not content with their own tradition? Because of the difficult situation which France occupies in the modern world, I believe. Her fall from her traditional position of power and eminence has shocked the French out of their isolation and driven them to an "agonized reappraisal" of their traditions and beliefs. Naturally they flounder about and go a-whoring after strange gods and stranger philosophies. The rise of existentialism is only one symptom.

Another evidence of the spiritual incertitude of the French is their search for outside sources of influence upon their own thinkers. Delay has pointed out that Jackson considerably influenced Ribot, Janet's predecessor at the Collège de France, but there is little evidence of direct influence of Jackson on Janet. In his own account of his psychological development, Janet derives

his ideas from Maine de Biran through Jouffroy, Moreau de Tours and Baillarger. Jouffroy was a contemporary of Herbert Spencer from whom Jackson says he derived his guiding principles. I cannot point to a contemporary German source, since I am not sufficiently familiar with German philosophy, but I am quite confident that such exists. It is just another indication that, at certain epochs, ideas are floating about throughout the intellectual world.

As the French look about for extraneous sources of their own dynamic tradition, because they are uncertain of themselves and of their place in the modern world, they are not long in running across apparent deficiencies in Janet's work. One has been variously expressed, usually that Janet does not realize the importance of positive forces, largely instinctual, and insists too much on negative factors. Here is where the modern eclectics think Jackson comes in, who wrote that the symptomatology of nervous disease is a double condition—there is a negative and there is a positive element in every case —and that disease only produces negative mental symptoms answering to the dissolution, all elaborate positive mentally symptoms being the outcome of activity of nervous elements untouched by any pathological process. Here he overstated his case, since epileptic attacks and hallucinations are positive symptoms produced by intoxication or irritation, therefore not by elements untouched by pathological process. In general, however, the distinction between positive and negative symptoms is valid and fruitful. Is this concept unknown to Janet? Obviously not, since the emergence of released positive symptoms may be produced either by weakening of the controlling forces or by strengthening of the suppressed ones. In his studies of psychological force he talks constantly of these forces. Still, he did stress the negative aspect. But why should this be held against him so strongly as to rule him out from any part in the instruction of younger psychiatrists? Since when are negative factors unimportant in etiology? Need I remind you of insulin and vitamins?

The difference of approach by Freud and Janet seems to have been, as one might suppose, a matter of temperament and training. Freud, a very sick man most of his life, was interested mainly in understanding the impulses surging out of his own tortured unconscious. Untrained in logic and philosophy, he elaborated, prematurely, explanations in terms of traditional methods of thinking, mingling inextricably with the scientific concepts he had been taught during the immediately preceding years. Janet, normal affectively, highly trained in logic and philosophy, followed the French tradition derived from Jouffroy, who laid down the method to follow in 1833. "One conceives two methods of constructing a science of the intellectual and moral world. The first consists of starting from questions and then searching in the consciousness for those facts of human nature related thereto and alone able to clarify them. It is in this way that philosophy has always proceeded to our day. The second would consist in observing and determining, first, all the facts of human nature, without regard to questions; then, when psychology would be constructed with the data which were thus gathered, one would proceed to the questions, and one would see what science could answer with certainty. This second method is a modern invention; the idea of making the phenomena of the human spirit the object of a science of methodical and regular observation, entirely independent of the solution of philosophical questions, even in the interest of these questions, was not conceived before our time. . . ."

Janet faithfully followed the second method all his life. That Freud followed the first is abundantly evident throughout his work. That he sought for data to support his beliefs, intuitively arrived at, is proved by his letters to Fliess. His long and serious illness gave him insight but led him often into error. Let us take time to examine the matter of the perponderant importance of sex in the origin of neuroses.

We know very little of the sexual life of either Freud or Janet. Freud, who was so keen to uncover the sexual life of his patients, has revealed very little of his own. He never made a frank confession comparable with that of Reik. Janet tells us in his autobiographical sketch how he lost his religious faith when a youth but mentions no sexual trauma. Freud, on the contrary, gives many hints of his obsession with sex, during his long betrothal, such as returning twice to the redlight district in an Italian town. It is probable that during this period he was masturbating and feeling very guilty about it; at least, that is the logical conclusion to be drawn from the facts that in his letters to Fliess he complained about his hysteria (Letter 70) and later makes repression of masturbation the casual factor (Letter 72). All we know about Janet during a similar period of his life is that he was a gay young blade very much in demand at dances and parties all up and down the coast of Normandy. If sexual impulses troubled Janet during this time I am quite persuaded that he handled them in the traditional Latin way by fornication and felt no guilt over the matter. To Janet sex would be no monster breathing fire and disaster from the subterranean caverns of the unconscious. The French slew that monster in the 13th century, when Simon de Montfort massacred 400,000 Cathari in the south of France, not, unfortunately, before they had imposed celibacy on the clergy. After that holocaust sexual appetite has never been considered by most of the French in any light other than hunger, thirst, or any appetite.

It is understandable, therefore, that Freud should give such prominence to the instinctual individual factors and their conflict with the cultural, social factors in mental life. It is understandable also that his theories were first appreciated, in France, in the south, where the old puritanical tradition had never completely died out. Nor were they completely rejected by Janet. He even proposed that those cases in which the intrapsychic conflict seemed to be the most important causative factor be called the "syndrome of Freud." This naive suggestion, of course, infuriated the disciples of Freud.

Janet was repelled by Freud's work, not because it was dynamic; his own was equally so but with different emphasis. One thing which repelled Janet was the illogical form in which Freud's writing is cast. To a mind highly trained in logic and philosophy, as was Janet's, it must have been as painful as an instrument out of tune to the conductor of an orchestra who possesses absolute pitch. It continues to distress the French mind. Even such a sympathetic critic as Madeleine Cavé writes, "Freud has baptized 'psychoanalysis' a horrible mixture of observations of facts, scientific theories, hypotheses without any relation to the observation of neuroses, unverifiable phylogenetic explanations, with numerous errors of judgment and reasoning." It is true that she goes on to write: "Suppressing the nocive role of the infantile pathogenic memories, the neurotic sees his morbid symptoms disappear. The proof is then made that repressed infantile sexual emotions were the cause of the neurosis." Had she been a physician, she would never have fallen into such a hoary *post hoc ergo proper hoc* argument. It is evident that Madeleine Cavé has a deep psychological need to believe, which might distort her judgment, but only in favor of Freud, be it noted. Freud's feeble grasp of locial principles has been a major catastrophe for scientific psychology.

Another element in Freud's work which made it distasteful to Janet is his anthropomorphic manner of expressing his ideas. This results in mental pictures of three warring little men in the head and memories from childhood of Milton and the wars of God and Lucifer. You may remember that Freud was very fond of Milton's "Paradise Lost" and turned to it for consolation when he quarreled with Martha. This is why Freud's psychology seems to most people so dynamic, so alive, whereas Janet's seems cold and calculated, like figures in

a ledger. To one type of mind only warring personalities seem dynamic.

No, the neglect of Janet is not because his psychology is not dynamic. We must search further.

(5) *Janet Is a Materialist.*—Here I believe we get closer to the root of the matter. As a priest once remarked, *C'est un matérialiste de gros ventre.* Of course, Freud claimed to be an atheist, but his thought is cast in a theological mould. This was evident to me when I first read him. It has been remarked also by many others. Way, for example, has written: "[Freud's] dualism, and that of the whole of this [psychoanalytical] science, is no doubt theological in derivation, an involuntary continuation of the habit of mind which produced the Heaven-Hell antithesis and the medieval antithetical outlook in general."

And Boring notes: "Dynamic psychology seems to fit more readily than other psychologies into the milieu of the Catholic Church which, being concerned with human responsibility, is especially interested in the nature of human motives." So much is this true that we see today an interesting attempt to absorb psychoanalysis into the traditional corpus of Crdistian philosophy in the works of Nuttin, Schwartz, Stern, and others. Certainly the emphasis on sex is not of at nature to repel the Church which of a nature to repel the Church which has had desperate struggles with it through the centuries and the strife is not ended. Witness what is going on in Ireland, where, says O'Falain, "what we need, surely, is the lifting of an unclean cloud." At least one attempt has been already been made (Sanders) to rewrite Freudian phychology, with God aded. Of course, Freud called himself an atheist, but the Church has never denounced him, or Janet, for that matter. The Church worries about heretics, not atheists, knowing that ninety-nine per cent of human beings are incurably religious. Since Jackson specigcally accepts the dualistic viewpoint, he may be dismissed immediately, but Janet's exposition is monistic, and the real conflict between him and Freud is between the spiritualistic and the materialistic viewpoints. In this Janet was following consistently the main line of French descent from Jouffroy, as we have previously pointed out, and from Condillac, of whom it was said that he was no materialist, but his work was rigidly materialistic.

As a matter of fact, both Janet and Freud were greatly influenced by religion. You may remember also, that, as a young child, Freud used to accompany his nurse to Catholic services and, on his return, lecured his parents on the doings of God. Not only is Freud's thought cast in areligious mould (if we define religion as the cultivation and propitiation of occult powers personified), but he was much preoccupied with it because it deals with the eternal mysteries in which any intelligent man must be interested. Although Freud denied that he had any faith, he wrote in his "Moses and Monotheism" that he envied those who had and identified homself with Moses. And Janet, after telling how he lost his faith during his youth, continues: "It was a question of conciliating scientific tastes and religious sentiments, which was not an easy task. The conciliation could have been effected by means of a perfected philosophy satisfying both reason and faith. I have not found this miracle but I have remained a philosopher." And so he built up his system on a consistently objective monistic basis, but continued to be preoccupied with such questions as religious ecstasy and doubt. He was a mystic at heart but kept his tendencies out of his psychological thinking. Nevertheless, his eyes were turned rather toward Heaven. Freud, on the contrary, was thoroughly permeated by the doctrine of original sin, as was noted by his disciple Sachs. He was quite at home with St. Paul, who complained, "For the good that I would I do not, but the evil which I would not, that I do." He could not keep his eyes away from fascination with the deep dark recesses of his unconscious Hell. We should remember the lefthanded

compliment of Dalbiez—a sympathetic critic: "Freud's work is the most profound analysis that history has ever known of the less human elements in human nature." A rabbi at heart, he could think only in terms of a struggle between personalities, laid down the law to his disciples, and cast them off when they disagreed with him.

And this is, to my mind, a major reason for Freud's popularity. He is most popular among Jews and Christians of the Old Testament tradition who have lost their faith. When its main tenets come back to them in a pseudoscientific guise, it strikes them at once as truce because is repeats, in an acceptable terminology, their traditional forms of thinking. For this reason also Freud's psychology will continue to be popular, whereas Janet's—formal, logical, impersonal—will appeal to only a small group thoroughly permeated by the materialistic scientific approach. Freud will always be the more popular because mankind will not give up its most cherished Urdefense—that it possesses a soul, a spark of the divine fire, however infinitesimal, which governs its conduct. Neither of them, however, can compete successfully on the American scene with that other neurotic of genius, Mary Baker Eddy, who is more attuned to the prevalent pie-in-the-sky American philosophy.

(6) *Janet Was a Tragic Failure.*—Brachfeld wrote that "Pierre Janet is in a sense a tragic figure in the history of modern phychology. He reached the threshold of the promised land but, unfortunately, it was not granted him to enter it. He hesitated to take the decisive step, alarmed no doubt at the revolutionary tendency of his own theories." This is a purely gratuitous assumption, and we are not told what was the decisive step he dared not take.

If Janet was a tragic figure he was completely unaware of it. He was always bright, alert, friendly to everyone, and curious about everything. Freud was the tragic figure—somber, secluded, asocial, pessimistic. The accusation of Brachfield, however, does not have reference to their temperaments. He accuses Janet of missing the boat, and that there are things which he overlooked. What of it? Who has not? Freud perhaps? It must be remembered that the paradise Brachfield is speaking of is Adler's paradise, not Freud's. We may ask what was the decisive step which Janet failed to take? Of course, he was never much interested in the meaning of individual symptoms, but not because he feared their revolutionary tendencies. I hope that we have all advanced beyond the naïve idea that "Ye shall know the Truth and the Truth shall make you free." I have already indicated my belief that the fundamental difference between the two men is one of viewpoint and method. Lévy-Valensi once remarked that every time a discussion of pathogenesis separates the psychiatrists, one can be sure to find, in a form favored by the times, the opposed opinions of the spiritualists and the materialists.

There is another dichotomy in psychiatry among the materialists themselves, exemplified by the different theories of Janet and another of my teachers—de Clérambault—for the explanation of the systematized psychoses. Clérambault maintained that the fundamental precipitating cause was the phenomenon of echo of thought and maintained that no idealogy could ever explain it. Clérambault explained this by supposing histological structural alterations in the neurones, whereas Janet, who accepted Clérambault's description of the syndrome, almost intact, elaborated a functional explanation in terms of activities in the middle level of his hierarchy. We have there a dichotomy between the structuralists and the functionalists. It is evident, here again, that there is no conflict as to fact, only a clash of two ways of trying to explain the same facts. As Paulus puts it: "To conclude in two words, the psychological theories are incapable of proof, the physiological theory has not furnished any."

And this brings me to my final theme, the physiological-psychological dichotomy. Neither Freud nor Janet was a biologist

at heart. I know that people have tried to make a great neurologist out of Freud; their efforts are unconvincing; a good neurologist he was but not a great one. He was unsuccessful in physiology and a failure as a chemist. He knew very well that he was essentially a visionary and wrote so to Fliess. I am quite persuaded that Brücke knew this and that this was the real reason why he advised Freud to abandon biology, softening the blow to Freud's pride by placing this advice on an economic basis. Janet, likewise, although he worked transitorily in a physiological laboratory in his youth, on the insistence of his uncle, remained a philosopher. Now both Janet and Freud realized that their psychological theories did not adequately account for any of the phenomena which they tried to explain, that their solutions were largely verbal. This was as true of Janet as of Freud. Cavé writes: "Even Pierre Janet explained the unsciousness of certain memories by giving a name to his phenomenon. He states that there exists in man a superior faculty realizing the synthesis of all the perceptions which he has at any one moment of all the memories which he has acquired. This faculty of synthesis he supposed to be impaired in hysterical patients. This is merely expressing his findings in other words." One is reminded of Franz Joseph Gall, who wrote (Vol. 4, p. 330): "Give animals fundamental faculties and you have the dog who chases *passionately*, the weasel who strangles chickens with *fury*, the nightingale who sings beside his mate with *passion*." These faculties are only words, names for facts of observation which they are supposed to explain.

The analysts deal also largely with words. That some psychoanalysts subconsciously realize this verbalism is evident from many slips of the tongue which I have overheard. I have quite a collection of them which time does not permit me to relate. And I am not one to belittle the power of words, for good and for evil. "In the beginning was the Word." Words are information on which the functioning of the neocortex depends. But that is not what I am talking about. I am talking about verbal explanations which merely translate words into other words. Both Janet and Freud knew that they offered only partial explanations of the phenomena they described. Freud remarked to Joseph Wortis, "Psychoanalysis never claimed that there were no organic factors in the psychoses. I said that analysis is not everything. There are other factors—the dynamic factors—what we call the libido—which is the drive behind every neurosis. Psychoanalysis cannot influence that because it has an organic background. It is the biochemist's task to find out what that is, and we can expect that the organic part will be uncovered in the future. So long as organic factors remain inaccessible analysis leaves much to be desired." And Janet remarked in discussing schizophrenia that he expected the secret of this malady to be discovered by the chemists. While I do not doubt either the existence or the importance of psychic and social factors in the genesis of mental disease, I never cease to be amazed at the amount of psychic trauma that the normal person can absorb, and we must never forget that a patient's behavior may be abnormal because his brain is sick.

Etiological chemical substances have not been indentified, but there are many indications that such will be found. Loewenhart's experiments with carbon dioxide pointed the way, however far his successors have strayed from it. The effects of toxins on mentality have long made it certain since Moreau de Tours wrote about hashish. The newer studies on lysergic acid, anticholesteinases, reserpine (Serpasil), and other drugs give us hope. Lately adrenochrome indicates a possible source in the body. If and when these etiological chemical factors are indentified, the work of both Janet and Freud will be as neglected overnight by the physicians as are the psychological factors in general paresis. And unjustifiably so, since the mechanisms which they have so laboriously elucidated will continue to operate as long as mankind exists. I am

quite convinced that psychogenetic factors play a role in the genesis of many mental disorders—a role which varies in importance from hysteria at one to schizophrenia at the other extremity of the gamut. If I talk seldom of these factors it is for the same reason which Freud gave for neglecting the biological factors—because others talk enough of them.

I conclude, therefore, that Freud and Janet are the two great men who led psychology out of the ivory towers into the clinic. Much has been made of Freud's courage in defying the opposition of the Viennese medical profession. Personally, I think he unnecessarily created much of what he suffered. Janet, also, needed courage of no mean order to stand up alone in opposition to the towering figure of Bakinski, in all the pride and arrogance of his world-wide reputation, when all his colleagues had been reduced to silence, and tell him that, imaginary or not, the patients had troubles and something should be done about them. Both Janet and Freud developed under the stimulus of Charcot, who said in one of his Tuesday clinics in 1885: "Until the present time we have been used to set psychology aside or teach it only in college, but then it was only a feeble rosescented psychology of little use. To know only that we have various faculties is not very useful in application. It is another psychology which we must create, a psychology reinforced by studies of pathology such as we are undertaking."

As dynamic psychology becomes constructive it will incorporate the best concepts of the two men, and both will be looked upon as stellar figures in the psychiatric firmament. I was very interested to read recently, in the report of the Conference on Psychodynamic Principles of the American Psychiatric Association, the following: "As a frecipitating factor, conflict in excess of an individual's current integrative capacity plays a highly important role in the production of neurosis and psychosis. The converse of this principle is that whatever reduces integrative capacity may serve as a precipitating factor by increasing the possibility of being overwhelmed by frustration or conflicts hitherto managed successfull." The first sentence is Freudian, the second Janetian, integrative capacity being only a paraphrase of Janet's faculty of synthesis. This prophetic *rapprochement* of Janet and Freud is signed by two eminent local psychoanalysts—Thomas French and Maxwell Gitelson. But we must remember that neither Freud nor Janet reached definitive formulations. Much has been made of the tentative manner in which Janet presents his theories; we should remember that Freud said that he did not know how much he believed of what he had written.

Much has been made also of the epidemic of convulsions which Charcot provoked in his hysterics and of the epidemic of multiple personalities which Janet provoked. We should not forget, also, the epidemic of incestual fantasy which Freud provoked in his patients. Both Janet and Freud were investigators rather than therapists. Janet gives his meager results in his great treatise on psychotherapy, and Freud remarked at the end of his life that psychoanalysis would be remembered as a theory of the unconscious and not as a method of therapy. I do not need to add in Chicago that what is called psychoanalysis today bears less and less resemblance to Freud's technical procedures, so that one wonders what justification there is for speaking of the present dynamic formulations as psychoanalytic. This should surprise no one, since the analysts have not been able to formulate a definition which is acceptable even to a small group.

I have not attempted to weigh Janet and Freud in a balance; my bias is obvious. My purpose has been to lift Janet up again into the field of vision of the psychiatrists and, perhaps, induce a few of them to take a good look at him—all of him—not just his beginnings. They will be repelled at first by a phraseology very different from the analytical one to which they are accustomed, but, if they persist beyond such superficial

barriers, they will find the effort rewarding.

It seems to me, then, that the theories of Janet and of Freud represent two common ways of looking at man and his relation to the world; whether you prefer the one or the other is largely a matter of taste, since there is no proof available or possible for either. Meanwhile, I believe Freud was right when he remarked to Wortis: "The relation of the physical and mental states—that is the field of work in the future." And Janet wrote: "The most useful psychology of the future will be a practical psychology of conduct which will at the same time be dynamic and will study the physiological production of energy and its distribution." That s why I back the chemists and get biochemical laboratories built in our state institutions.

I submit that it is time we ceased to preoccupy ourselves with what Freud called the mythological part of his work, with Eros and Thanatos, with the Superego, Ego and Id. Nor is Janet's work free of mythology, as Dumas complained on more than one occasion. If we must live by a myth I see no reason to prefer the pessimistic Freudian or the indifferent one of Janet to the optimistic Christian myth. Rather let us work on what Freud said to Wortis was the important problem for the future—the relation of the physical and mental states. This is, of course, psychobiology. That it should appeal to me will not surprise you when you remember that one of my teachers was C. Judson Herrick, a collaborator and life-long friend of Adolf Meyer.

This advice we are able to follow today in ways undreamed of by Freud and Janet, children of their time. Not only has biochemistry made gigantic strides, but a new tool has become increasingly illuminating, the electronic amplifier. We now begin to see that there are two systems of neurones in the brain: a diffuse one, inept for the transmission of signals but very important for our affective life, and another which can be understood only by the light of modern developments in communication-engineering. Janet would be delighted by these developments and would undoubtedly weave them into his theories of psychological force and tension so much more adequately than he could the cruder mechanics and chemistry of his day. His later work is full of "feedbacks"—called by other names, of course.

I apologize to the members of this Society for presenting these fragmentary comments to you, although I really owe you no apology, since you brought them on your own heads by electing me your president. I should never have dared to do so except that you probably will not take them seriously, since you know that I have had only a self-analysis. I am, therefore, a child of the darkness, whereas "Ye are all children of light." And I thank you for forcing me thus to think again about these patients and their troubles because the neurotics, like the poor, we shall always have with us, and someone must care for them. And I am now in a position where I must take part in decisions as to how they can best be managed. Finally, I am glad to have had this opportunity to call your attention again to one of the greatest thinkers of all time in the field of abnormal psychology—Pierre Janet.

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A Comparative Study of Reserpine, Chlorpromazine, and Combined Therapy

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In recent months increasing use has been made of reserpine, chlorpromazine, and combined reserpine-chlorpromazine therapy in psychiatric disorders. As these therapies have gained in popularity, there has been an urgent need for adequate comparative studies in order to determine the indications for each therapy. It was with this purpose in mind that the present study, which has extended over a 20-month period, was undertaken.

Subjects

This study was conducted in a hospital building housing 740 chronically disturbed psychotic female patients. Three comparable groups of 150 patients each were selected. They were chosen chiefly for their excited, hyperactive, assaultive, or destructive behavior, regardless of diagnosis, age, duration of illness, or previous treatment.

One group of 150 patients was treated with reserpine alone for three to six months. Another group of 150 patients was treated with combined reserpine-chlorpromazine for three to seven months. The findings in these two groups have been reported in detail in previous papers * and will be merely summarized in this paper. The final group of 150 patients was treated with chlorpromazine alone for three to seven months. The latter group is reported for the first time in this paper and will, therefore, be analyzed in greater detail.

The majority of the patients had already received courses of electroconvulsive and/or insulin coma therapy without satisfactory or lasting results. All of the patients in the study were started on drug therapy at a time when they were disturbed. If they had previously benefited from insulin coma or electroconvulsive therapy, they were allowed to relapse before drug therapy was instituted. While on reserpine, chlorpromazine, or combined therapy, the patients received no other somatic therapy and no other sedative, with the exception of anticonvulsant medication in a few epileptic patients. Since the patients in all three groups were scattered equally throughout the 10 wards of the building, each group was subjected to the same environmental influences.

Dosage

The dosage plan for the use of reserpine alone was as follows: When starting therapy the patient received 5 mg. of reserpine intramuscularly and 3 mg. orally each morning. The oral dose remained the same until the close of therapy. The intramuscular dose was continued for 10 days. If by this time the patient was showing a beneficial response (not merely sedation), the intramuscular dose was given every other day for three doses. Then, if the pa-

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The reserpine used in this study was supplied by Ciba Pharmaceutical Products, Inc., under the name of Serpasil. The chlorpromazine was supplied by Smith, Kline & French Laboratories, under the name of Thorazine.

* References 1-5.

tient's condition still showed evidence of improvement, the intramuscular dose was given every fourth day for two doses. Finally, if the patient's mental state remained favorable, the intramuscular dose was discontinued as a regular medication and was given only as a booster dose at such times as the patient became very disturbed.

If after the first 10 days of oral and intramuscular reserpine therapy the patient did not show a beneficial response, the oral and intramuscular dose was continued for six more days. If there was still no improvement, the intramuscular dose was increased to 10 mg. every other day and 5 mg. on alternate days. This regimen was carried on for eight days. If there was still no improvement, the intramuscular dose was raised to 10 mg. daily for five doses. If at the end of this time no improvement was evident in the mental state of the patient, the intramuscular dose was reduced to 5 mg. daily for three days and then eliminated completely, whereas the daily oral dose of 3 mg. was continued.

A maintenance oral dose of 3 mg. was found to be optimal in most of the patients. However, in some patients the maintenance dose had to be reduced to 2 mg. or occasionally to 1 mg. because of side-reactions.

The following dosage was used in combined reserpine-chlorpromazine therapy: The patient was started on 3 mg. of reserpine and 25 mg. of chlorpromazine orally once a day. After 10 days the chlorpromazine was increased to 25 mg. twice a day. At the end of three to four weeks, if the patient was not showing satisfactory progress, the dose of chlorpromazine was increased to 50 mg. twice a day, reserpine remaining at 3 mg. daily. After another three to four weeks, if the patient's therapeutic progress was still unsatisfactory, 5 mg. of reserpine intramuscularly was added to the oral regimen. This was continued for 10 days. If the patient then showed signs of responding to therapy, intramuscular medication was gradually withdrawn, but the oral medication remained unchanged until the close of therapy, when it was slowly discontinued. If, however, after 10 days of intramuscular injections the patient was not showing an adequate therapeutic response, the intramuscular dose was raised to 10 mg. and was continued until the response was adequate; then intramuscular injections were gradually withdrawn, leaving only the oral medication. A course of therapy lasted a minimum of three months.

If at the outset the patient was extremely disturbed and an early quieting effect was necessary, the patient was started on 5 mg. of reserpine intramuscularly and 3 mg. of reserpine and 25 mg. of chlorpromazine orally once a day. After 10 days the chlorpromazine was increased to twice a day, and if the patient's progress was satisfactory the intramuscular injections were gradually withdrawn. However, if progress was still not satisfactory, the injections were continued for another 10 days. Then if necessary, the intramuscular dose was raised to 10 mg. After improvement was sufficient to discontinue this initial course of intramuscular reserpine injections, the subsequent dosage regimen was the same as outlined in the preceding paragraph.

In treating with chlorpromazine alone there was much greater latitude in the dosage schedule, for there was considerable variability in the individual needs of the patient. The dose was usually started at 25 mg. three or four times a day and was increased rapidly in the first 10 days up to 400-600 mg. a day in four divided doses. If after two weeks at this dose level the patient was not showing sufficient improvement, the dose was raised by increments of 200 mg. a day every five or seven days until a satisfactory clinical response was reached. Although the highest daily dose was 1800 mg., the majority of patients required no more than 600 mg. a day. After a satisfactory clinical result had been obtained, the dose was allowed to remain at this level for two or three weeks and then was gradually lowered to 200-400 mg. a day, being kept at this dose for about six

or eight weeks. The drug was then gradually withdrawn. The entire course of treatment lasted a minimum of three months. The patients in this study were treated from three to seven months.

Results

The categories of improvement used in the study are defined as follows: By "markedly improved" is meant that the patient's mental state and behavior have improved to such an extent that with a normal amount of supervision she would be able to adjust adequately outside of a hospital; delusions and hallucinations can no longer be elicited. By "moderately improved" is meant that, although the patient is not well enough to live outside of a hospital, her behavior has improved to the extent that she is now usually cooperative and is adjusting fairly well to the hospital environment. By "slightly improved" is meant that the patient is a little easier to manage, but still manifests excited, assaultive, or destructive behavior. The evaluation of the patient in regard to degree of improvement was made by the physician in charge (J.A.B.), the supervising nurse of the building, and the nurse or attendant in charge of the patient's ward.

Tables 1, 2, and 3 are an analysis of improvement according to diagnosis in the

TABLE 1.—*Improvement with Reserpine in Respect to Diagnosis**

Diagnosis	Markedly Improved	Moderately Improved	Slightly Improved	No Improvement	No. of Cases
Dementia praecox, paranoid	4	2	10	3	29
Dementia praecox, catatonic	17	27	13	11	68
Dementia praecox, hebephrenic	1	8	6	4	19
Dementia praecox, mixed	4	4	1	1	10
Dementia Praecox, total	26 (20.6%)	51 (40.5%)	30 (23.8%)	19 (15.1%)	126
Manic-depressive, mixed	1	1	1	----	3
Involutional psychosis, melancholia	1	1	----	1	3
Involutional psychosis, paranoid	----	4	----	----	4
Psychosis with mental deficiency	3	----	----	3	6
Psychosis with cerebral arteriosclerosis	----	----	----	1	1
Psychosis with cardiorenal disease	1	----	----	----	1
Epileptic psychosis, epileptic clouded states	----	1	2	----	3
Epileptic psychosis, deterioration	----	----	1	----	1
Alcoholic psychosis, Korsakoff's	----	1	----	----	1
Primary behavior disorders, simple adult maladjustment	----	----	1	----	1
Total	32 (21.3%)	59 (39.3%)	35 (23.3%)	24 (16.0%)	150

* Barsa & Kline.[1]

TABLE 2.—*Improvement with Combined Reserpine-Chlorpromazine in Respect to Diagnosis**

Diagnosis	Markedly Improved	Moderately Improved	Slightly Improved	No Improvement	No. of Cases
Dementia praecox, paranoid	5	13	11	3	32
Dementia praecox, catatonic	9	16	22	6	53
Dementia praecox, hebephrenic	1	2	7	2	12
Dementia praecox, simple	----	----	1	----	1
Dementia praecox, mixed	6	6	8	----	20
Dementia praecox, total	21 (17.8%)	37 (31.4%)	49 (41.5%)	11 (9.3%)	118
Manic-depressive, mixed	5	1	----	----	6
Involutional psychosis, melancholia	3	----	1	----	4
Involutional psychosis, paranoid	2	3	2	1	8
Psychosis with mental deficiency	1	4	1	----	6
Psychosis with psychopathic personality	2	----	----	----	2
Psychosis with cerebral arteriosclerosis	----	1	1	----	2
Psychosis with cerebral embolism	1	----	----	----	1
Psychosis due to epilepsy, deterioration	----	1	----	----	1
Psychosis due to alcohol, acute hallucinosis	----	1	----	----	1
Psychosis with syphilitic meningoencephalitis	----	----	1	----	1
Total	35 (23.3%)	48 (32%)	55 (36.7%)	12 (8%)	150

* Barsa & Kline.[1]

TABLE 3.—*Improvement with Chlorpromazine in Respect to Diagnosis*

Diagnosis	Markedly Improved	Moderately Improved	Slightly Improved	No Improvement	No. of Cases
Dementia praecox, paranoid	5	14	16	4	39
Dementia praecox, catatonic	10	9	19	4	42
Dementia praecox, hebephrenic	1	3	6	1	11
Dementia praecox, simple	----	----	1	----	1
Dementia praecox, mixed	8	2	6	3	19
Dementia praecox, total	24 (21.4%)	28 (25%)	48 (42.9%)	12 (10.7%)	112
Manic-depressive, mixed	7	3	1	----	11
Involutional psychosis, melancholia	3	----	1	----	4
Involutional psychosis, paranoid	2	2	1	1	6
Psychosis with mental deficiency	1	1	----	1	3
Psychosis with psychopathic personality	1	1	----	----	2
Psychosis with syphilitic meningoencephalitis	----	----	1	----	1
Psychosis due to epilepsy, epileptic clouded states	1	1	3	1	6
Psychosis due to epilepsy, deterioration	----	1	4	----	5
Total	39 (26%)	37 (24.7%)	59 (39.3%)	15 (10%)	150

three comparable groups of patients who were treated with reserpine, combined reserpine-chlorpromazine, and chlorpromazine, respectively. It can be seen that the degree of improvement is not significantly different in the three groups. Table 4 analyzes the improvement of the chlorpromazine-treated patients according to age. In contrast to the patients receiving reserpine and combined therapy, there was a tendency in the chlorpromazine group for the younger patients to show a greater response to therapy. However, since most of the older patients had been ill for a longer period of time, the duration of illness rather than the age may have been the determining factor in their poorer response to therapy. Tables 5 and 6 are a further analysis of the improvement in the chlorpromazine-treated patients according to the duration of the present hospitalization and the duration of the illness. Although in all three groups it was found that the longer the patient had remained in the hospital and the longer she had been ill the less were her chances of achieving a marked improvement, this was especially so in the patients treated with chlorpromazine alone. For example,

TABLE 4.—*Improvement with Chlorpromazine in Respect to Age*

Age	Markedly Improved	Moderately Improved	Slightly Improved	No Improvement	No. of Cases
15–20	2	1	----	1	4
21–30	12	4	7	2	25
31–40	12	12	16	4	44
41–50	7	12	20	4	43
51–60	5	6	13	3	27
61–68	1	2	3	1	7

TABLE 5.—*Improvement with Chlorpromazine in Respect to Duration of Present Hospitalization*

Duration of Present Hospitalization, Yr.	Markedly Improved	Moderately Improved	Slightly Improved	No Improvement	No. of Cases
Less than 1	13	----	1	1	15
1–3	21	6	7	3	37
3–5	4	8	4	1	17
More than 5	1	23	47	10	81

TABLE 6.—*Improvement with Chlorpromazine in Respect to Duration of Illness as Measured from Time of First Hospitalization*

Duration of Illness from First Hospitalization, Yr.	Markedly Improved	Moderately Improved	Slightly Improved	No Improvement	No. of Cases
Less than 2	15	2	4	2	23
2–4	7	4	5	1	17
4–10	12	12	16	7	47
More than 10	5	19	34	5	63

of the patients receiving reserpine or combined therapy, 5% who were in the hospital more than five years showed marked improvement, whereas only 1% of such patients treated with chlorpromazine alone were markedly improved.

Clinical Course

In a previous report† one of us (J.A.B.) distinguished three stages in the patient's course of therapy with reserpine alone: The sedative period, the turbulent period, and the integrative period. The sedative period began very soon after the start of therapy, and, as the name implies, was characterized chiefly by the sedative effects of the drug, the patient becoming quieter, less disturbed, and rather drowsy. This was followed by the turbulent period, in which the patient's behavior became more disturbed and the delusions and hallucinations were often more pronounced. Tremulousness, restlessness, mounting tension, and anxiety were prominent symptoms. The patient frequently complained of feeling strange, not like herself, and feeling at times that she had no control over her impulses. The successfully treated patient then passed into the integrative period, in which she became more cooperative, more friendly, and more interested in her environment. Delusions and hallucinations gradually faded until they seemed to disappear.

In combined reserpine-chlorpromazine therapy these three stages in treatment were also evident, with certain differences.[5] The sedative period was more pronounced, longer in duration, and tended to overlap the subsequent stages, so that not infrequently a patient in the integrative period would also complain of drowsiness, lethargy, and a sense of fatigue. The turbulent period, on the other hand, was not as severe or as protracted as in uncombined reserpine therapy. As a result the course of therapy was less stormy and less distressing to the patient. Finally, in combined reserpine-chlorpromazine therapy the integrative period was much more gradual in onset and slower in progress.

In chlorpromazine therapy these three stages could not be clearly distinguished. Sedation was manifested early, but the patient did not usually pass through a real "turbulent phase." Integrating effects in the personality were often seen earlier than in reserpine or combined therapy. An important difference in the clinical course of chlorpromazine therapy was that the patient usually had a greater sense of well-being than with reserpine or combined therapy. In the latter therapies, the patient, even when showing clinical improvement, would not infrequently beg to have the drug discontinued, because of a persistent jittery feeling, or because of marked retardation of mental processes, or because of a sense of having been drained of all affect. These complaints were not common in chlorpromazine therapy.

Side-Reactions

The side-reactions observed in the patients treated with reserpine alone can be summarized as follows:

1. Side-reactions occurring early in therapy and usually disappearing spontaneously without reduction of dosage: generalized tremulousness, increased salivation, dizziness, convulsive seizures, drowsiness, sense of fatigue, abdominal cramps, diarrhea, nasal stuffiness, edema of face and feet, pins-and-needles sensations in the extremities.

2. Side-reactions occurring a little later in therapy and requiring reduction of dosage: anorexia following an earlier increase in appetite; an organic type of mental confusion; the development of a typical Parkinsonian syndrome. With reduction of dosage these symptoms disappeared.

Various drugs were used in an effort to combat the side-reactions of reserpine therapy. Atropine was used with varying success against the tremulousness. Oxphenonium (Antrenyl‡) bromide, an anticholinergic substance, was very effective

† References 1 and 2.

‡ Ciba Pharmaceutical Products, Inc.

against the abdominal symptoms. Phenylephrine (Neo-Synephrine) hydrochloride, ephedrine, or naphazoline (Privine) § nose drops were used to alleviate the nasal stuffiness. Amphetamine derivatives were useful in counteracting the drowsiness and sense of fatigue when they became very severe. However, most effective against the tremulousness, the restlessness, and the feelings of tension, which were especially acute during the turbulent period, was benztropine (Cogentine)‖ methanesulfonate, a synthetic anti-Parkinsonism drug with antihistaminic and anticholinergic properties. Benztropine was also effective against the symptoms of Parkinsonism when they developed.

The side-reactions with combined reserpine-chlorpromazine therapy were very much the same as those with reserpine alone, except that they were less severe, especially the symptoms associated with the turbulent period. However, in addition to the side-reactions attributed to the reserpine effect were those resulting from chlorpromazine, such as skin eruptions, jaundice, and agranulocytosis.

Of the 150 patients treated with chlorpromazine alone, 8 developed a generalized maculopapular eruption, 1 developed jaundice, 10 showed the typical signs of Parkinsonism, and 1 patient, who had had a lobotomy several years previously, went into status epilepticus. The skin eruption did not require the discontinuation or reduction of dosage, whereas the drug was discontinued in the patient who developed jaundice. The jaundice occurred after four weeks of therapy. The Parkinsonism was made to disappear either by reducing the dosage of chlorpromazine or, in some cases, merely by the addition of benztropine. The status epilepticus was controlled with amobartital (Amytal) sodium and the withdrawal of chlorpromazine. Chlorpromazine therapy was later reinstituted at a reduced dosage without the recurrence of convulsions.

§ Ciba Pharmaceutical Products, Inc.

‖ Sharp & Dohme, Inc., Division of Merck & Company, Inc.

Other side-effects of chlorpromazine included excessive drowsiness and sense of fatigue, especially in the early stages of therapy. When this symptom persisted and was severe, it was at times necessary to use amphetamine derivatives. Blurring of vision, dryness of the mouth, and an unpleasant taste were sometimes complained of temporarily during the early weeks of therapy. Edema of the face and feet was also an occasional early and transient symptom. In two patients there was engorgement of the breasts and lactation, but this disappeared spontaneously without reducing the drug. Photosensitivity of the skin was a common complaint, especially when higher doses were used, and it necessitated that the patients avoid exposure to sunlight. Constipation was very frequent, requiring the liberal use of cathartics. Increase in appetite and gain in weight were very common.

In this series of chlorpromazine-treated patients there were no instances of agranulocytosis, although among the patients treated with combined reserpine-chlorpromazine there were two cases.[6]

Promethazine (Phenergan ¶) hydrochloride (12.5 mg. once a day in the morning or, at times, twice a day in the morning and evening) was very valuable when used in conjunction with chlorpromazine. It seemed to increase the therapeutic effectiveness of chlorpromazine so that lower doses of the latter drug could be used, and thus many of the side-effects eliminated. Promethazine hydrochloride also often controlled the considerable restlessness shown by some patients receiving chlorpromazine. This restlessness was not usually associated with cramping or aching sensations in the extremities, as in reserpine therapy. Furthermore, contrary to the report of others,[7] promethazine hydrochloride was not found useful either in the treatment of Parkinsonism when it developed or in the direct prevention of Parkinsonism. It did allow the reduction of the dosage of chlorproma-

¶ Wyeth, Inc.

zine without sacrificing its therapeutic effect, and in this way (by using smaller doses of chlorpromazine) Parkinsonism could be prevented or made to disappear.

It was discovered that patients receiving reserpine, chlorpromazine, or combined therapy generally showed a reduced resistance to infection, so that at times a patient would become seriously ill from what started out as a minor infection. Therefore, it became the policy to treat all patients vigorously with antibiotics at the first evidence of infection.

Comment

From our studies it has become clear that it cannot be predicted with certainty which patient will respond best to which form of drug therapy. However, some general principles have been evolved which can be used as a guide in conducting therapy.

Combined reserpine-chlorpromazine therapy, as used by us, produces primarily an enhanced reserpine effect. It has other advantages over reserpine therapy. It has the advantage of not requiring intramuscular injections in most cases. Furthermore, the course of combined therapy is less stormy and less distressing to the patient because of a milder and shorter turbulent period. Thus, combined therapy has replaced therapy with reserpine alone, except in those cases that cannot tolerate chlorpromazine because of the development of jaundice or agranulocytosis.

The advantage of treatment with chlorpromazine alone is that the patient has a greater sense of well-being than with reserpine or combined therapy. Chlorpromazine therapy also seems most effective in the mental illnesses of shorter duration. Moreover, although depressions are more resistant to all forms of drug therapy, they tend to respond better to chlorpromazine alone.

On the other hand, chronic deteriorated schizophrenics, or chronic schizophrenics in whom apathy and withdrawal are predominant, do better on combined therapy. Also, since it has been found that a tolerance to chlorpromazine seems to develop after many months of treatment, those patients for whom maintenance drug therapy is expected for a long period should be given combined therapy. In this therapy the chlorpromazine can be gradually withdrawn and the patient maintained on reserpine alone.

Finally, those patients who refuse to take medication orally over an extended period are best treated with combined therapy, for in combined treatment only one injection a day is required, as compared with three or four a day in the case of chlorpromazine alone. It is possible to mix the reserpine and the chlorpromazine in the same syringe, as long as the injection is made immediately after mixing the ingredients.#

The indications for treatment with reserpine, chlorpromazine, and combined therapy are summarized as follows:

A. Chlorpromazine therapy:

1. Patients with mental illness of more recent origin, especially acute schizophrenia.
2. Patients in whom depression is a prominent symptom.
3. Patients who have failed to respond to combined reserpine-chlorpromazine.

B. Combined reserpine-chlorpromazine therapy:

1. Chronic deteriorated schizophrenics, or chronic schizophrenics in whom apathy and withdrawal are predominant.
2. Chronic schizophrenics in whom long-term maintenance therapy is anticipated.
3. Patients who refuse to take oral medication over a prolonged period.
4. Patients who have failed to respond to chlorpromazine alone.

C. Reserpine therapy:

1. Patients who have manifested jaundice or agranulocytosis in response to chlorpromazine.
2. Patients who cannot be followed closely in regard to side-effects of chlorpromazine (jaundice and agranulocytosis in particular).

Summary

Three groups of 150 disturbed psychotic patients, chiefly schizophrenic, have been treated with reserpine, combined reserpine-

This compatibility was not tested for brands of reserpine other than Serpasil.

chlorpromazine, and chlorpromazine alone under the same environmental conditions.

Of the patients treated with reserpine alone, 21.3% are markedly improved, i.e., discharged or ready for discharge; 23.3% of those treated with combined reserpine-chlorpromazine are markedly improved, and 26% of patients treated with chlorpromazine alone are markedly improved.

In all three modes of therapy the longer the patient has remained in the hospital and the longer she has been ill, the less is the probability of achieving a marked improvement. This is especially pronounced in the patients treated with chlorpromazine alone.

Chlorpromazine seems more effective in patients with mental illness of more recent origin, especially acute schizophrenia, and in patients in whom depression is a prominent symptom. Combined reserpine-chlorpromazine therapy appears more effective in chronic, deteriorated schizophrenics, chronic schizophrenics in whom apathy and withdrawal are predominant, and in schizophrenics in whom long-term maintenance therapy is necessary. Reserpine alone is indicated in those patients who have manifested jaundice or agranulocytosis in response to chlopromazine.

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Anxiety and Performance Changes with a Minimal Dose of Epinephrine

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Several investigators have demonstrated that an elevation in the level of circulating epinephrine accompanies psychological stress response and is associated with strong affective arousal.* It has also been commonly noted that a frequent consequence of epinephrine administered to man is anxiety and its physical accompaniments.[4] Nevertheless, despite these suggestions of an intimate connection between epinephrine action and human anxiety, surprisingly few studies have sought to develop the relationship further. Particularly neglected has been an approach to this problem in the context of broader considerations of personality functioning an dpsychological defense.

The present report describes a pilot experiment within a larger program of studies concerned with the reciprocal implications of psychological stress and disease and the functional activity of various endocrine systems. Its aim was to explore whether prolonged intravenous epinephrine infusion at a low dose level reactivated habitual idiosyncratic anxiety patterns in normal persons. The effect on certain indices of cardiovascular activity and on psychological and motor performance known to be disturbed in anxiety was also assessed.

Method

Subjects were 12 volunteer medical interns in good health, 10 men and 2 women, ranging in age from 24 to 28 years. Each underwent three occasions of evaluation. The first consisted of a one-hour clinical interview which focused on the subject's past history of stress and how he had previously experienced anxiety in terms of the development of conscious foreboding or dread and perceived somatic concomitants. Its purpose was to inventory the specific and unique symptoms emerging in situations of life stress. The second and third sessions were held on successive days approximately one week later and were devoted to epinephrine and saline (control) conditions arranged in counterbalanced order. Thus six randomly selected persons were given epinephrine first; the remaining six were administered a placebo as their initial substance. In all crucial respects the study employed a "double-blind" design. For each case there were two experimenters, one to elicit interview material and give the various performance tests, the other independently to prepare and administer the infusion, as well as obtain the cardiovascular readings. On both days the subject received identical treatment except for the solu-

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* References 1-3.

tion, which was unknown both to him and to the interviewer.

A typical session began with a five-minute interview concerned with the subject's contemporary feeling state. Next he was weighed and led into the testing room, where he reclined on a couch, and the blood pressure and pulse rate were recorded. An intravenous infusion of Solution 1 (isotonic saline) was started, using a Y-type drip apparatus, and permitted to continue for 8-10 minutes, while the subject adapted to the procedure. During this period further base-line blood pressures and pulse rates were taken at approximate two-minute intervals. A switch-over to Solution 2 was then made. On the control days the second solution also consisted of isotonic saline. On experimental occasions it contained epinephrine in such concentration that 5γ/kg. body wt/hr. was delivered. The epinephrine employed was Parke, Davis & Company's Adrenalin Chloride Solution. The pure epinephrine powder used in the preparation of this solution contains less than 0.1% arterenol (epinephrine).

The recumbent position was maintained for the next 20 minutes. Throughout this time careful observation and interview sought to evaluate the nature and extent of psychological and physical changes. Although the subject was instructed to report spontaneously whatever effects he became aware of, a prearranged set of questions regularly inquired into the arousal of anxiety or other affects, locus and type of somatic complaints, energy level, degree of discomfort, feelings of loss of control, and disturbances of body image. Further, when any changes did occur, were they from the person's subjective point of view old and familiar experiences or quite new and different? Blood pressure and pulse rate levels continued to be measured every two to four minutes in this stage as well.

Finally, the subject was seated upright and given a battery of tests in the following order:

1. *Critical Fusion Frequency.*—This task measures the subjective point at which a physically intermittent light is just perceived as a steady light. Employing the Halstead[6] apparatus and procedure, three blocks of five ascending runs were presented. Mean thresholds and estimates of variability (average deviations) were obtained for each block. In addition, the trend of successive threshold levels (slope) was crudely examined through a comparison of means for the first and third blocks to determine whether systematic change occurred with continued exposure to the flicker test.

2. *Hand Steadiness.*—The person was required to hold a stylus in the opening of a small circular hole in a vertical metal plate. As his hand wavered, the stylus touched the plate, activating an impulse counter. Score is the number of contacts within a 30-second period.

3. *Memory for Digits.*—The subtest of auditory digit span in the Wechsler-Bellevue Intelligence Scale[8] was used. Score is the total number of digits reproduced, i.e., forward plus backward.

4. *Physical Persistence.*—This procedure involved the continuance of a bodily posture in spite of fatigue and pain induced by that posture. The subject merely had to extend his preferred foot horizontally about 2 in. above the seat of a chair. Score is the time in seconds he could maintain this position before having to rest his leg.

5. *The Stroop Task.*[7] Three cards, each containing 100 stimuli, arranged in 10 rows with 10 stimuli per row, were administered successively to the subject. On the first card he was asked to read the names of various colors, such as red, blue, yellow, green, and brown, printed black on white. The second card presented squares actually tinted these colors, which he now was required to name. The third card listed the words of Card 1 randomly tinted in the colors of Card 2, with the restriction that tint and color name never coincided. The subject was instructed to continue as on Card 2 by naming the colors of the print only *as rapidly as possible.* The conditions of the last requirement were inherently stressful, since color name conflicted with color of print and the overlearned tendency simply to read the color name had to be inhibited. Score is the time in seconds necessary to complete the third card. Errors occurred too infrequently to warrant separate treatment as a measure.

6. *Motor Inhibition.*—A situation was adapted from the Downey Will-Temperament Scale[8] in which subjects wrote as one word the phrase "New Jersey Chamber of Commerce" within the boundaries of parallel lines ½ in. apart. Instructions were to write continuously and *as slowly as possible* without lifting pencil point from paper. Inhibition time is the number of seconds taken to complete the phrase.

7. *Word Fluency Under Distraction.*—Subjects had to list as rapidly as possible as many four-letter words as they could which began with a given letter of the alphabet. This was carried out under the distracting influence of raw noise. Different letters were used on each occasion. Two letters, *B* and *D,* were assumed to have roughly equivalent numbers of possible words, on the basis of entries in "Webster's New Collegiate Dictionary." These were randomly assigned to epinephrine or saline conditions. Score is the time in seconds to achieve a criterion of 12 words.

These procedures were chosen to sample a range of functions including sensory thresholds, motor performance, and intellectual control. During this testing phase blood pressure and pulse rate were recorded about every 20 minutes. A complete

session lasted approximately 90 minutes. Before being dismissed, subjects were urged to note any psychological or somatic changes during the next 24 hours and record their time of onset and duration.

Results

Symptoms.—The symptoms developed by each subject during epinephrine and saline conditions, as well as those occurring in ordinary situations of life stress as determined from initial clinical interview, are presented in Table 1. The categories describe all reported and visible changes and are an admixture of symptoms referring both to the organ affected and to the nature of the person's experience. For the most part the entries include subjectively perceived changes, although some of the phenomena were also objectively apparent to the observer, e.g., tremor, drowsiness, perspiration, and jaw tick. The material may be considered in two ways: first, a comparison of epinephrine and saline findings, and, second, their relation to previous anxiety reactions.

Mild apprehensiveness under epinephrine was described by seven subjects. The commonest subjective response, found in all persons, was a perception of heightened heart rate and/or heart beat. Yet a wide variety of additional symptoms were produced with both substances, saline as well as epinephrine: tightness, fullness or throbbing of the head; tremor or tremulousness; feelings of tenseness; fatigue, weakness, or drowsiness; abdominal sensations; perspiration, and flushes of warmth, among others. In general, these were mild to moderate in intensity.

However, epinephrine symptoms were distinctly more numerous and prominent. A total of 68 symptoms appeared in all epinephrine sessions combined; only 22 with saline. Moreover, with but one exception, all symptoms under saline were presented by the six subjects for whom this substance constituted the first trial and may be attributable largely to apprehensiveness in a still unfamiliar situation. Most persons did, indeed, spontaneously admit a greater uneasiness at the outset of the first occasion of testing. But it is striking that where a particular symptom developed with saline, it invariably also occurred under subsequent epinephrine, usually in more pronounced form. In each of the 16 instances in which an identical symptom obtained for both conditions and differences in degree between the two were discernible, the epinephrine response was severer and, according to our observations, generally more persistent.

The distinction between epinephrine and saline effects is also seen during the 24 hours following each type of treatment. Six persons reported a total of 12 symptoms, lasting from 10 minutes to 2 hours, after their epinephrine session. Included therein were headache, tremor, fatigue, irritability, palpitations, and tightness in chest. Of these, 10 symptoms were present in the reporting subjects during actual epinephrine infusion. By contrast, no untoward reactions were encountered subsequent to saline administration.

More impressive was a distinct tendency for epinephrine to produce personally patterned symptoms consistent with the subject's past history of anxiety. Thus, comparison in Table 1 of the kinds of symptoms evoked by epinephrine with those elicited in previous life stresses yields fairly substantial agreement. Of the 68 epinephrine symptoms, 53 accorded with those disclosed in initial interview as typifying a given person's usual anxiety response. Moreover, all epinephrine responses, whether mentioned earlier or not, were not felt by the subject to be unfamiliar experiences.

Further information on this point was developed in the course of informal post-experimental reviews of the study held with each subject. On these occasions all persons reaffirmed that their particular responses

TABLE 1.—*Habitual Anxiety Symptoms Revealed in Preexperimental Interview (I) and Symptoms Developed Under Epinephrine (E) and Saline (S) Conditions*

Subject	Apprehensiveness or Preoccupation	Headaches or Other Sensations in the Head or Neck	Tremor or Tremulousness	Feelings of Tenseness	Fatigue, Weakness, or Drowsiness	Palpitations	Abdominal-Visceral Sensations	Perspiration	Flushes of Warmth in Face or Abdomen	Other		
										Interview	Epinephrine	Saline
1	I	E	I E	I	I E	E						
2*	I **E**† S	**E** S	I E		**E** S	I E	I	I E S	I E S		**Dry mouth**	Dry mouth
3*	I E		I E	I **E** S		I E	I			Dry mouth; tightness in chest	Dry mouth; tightness in chest	
4	I E		E		I E	I E		I E	I E	Cold extremities		
5*	I		I E		I E	I E	I	I E	I E	Jaw tick; urge to defecate	Jaw tick	
6	I E	I				I E		I		Breath holding		
7*	I E S	I E	E			E	I E	I E S	I **E** S	Cold extremities; irritability	**Cold extremities;** dyspnea	Cold extremities
8*	I E	I E		I E	I E	E	I E	I E S		Tightness in chest; breath holding	**Tightness in chest;** breath holding	Tightness in chest
9*	I **E** S	I **E** S	I E	I **E** S		**E** S	I **E** S	I E S	I **E** S	Cold extremities	**Cold extremities**	Cold extremities
10	I	I	I E	I E		E	I E		I	Cold extremities	Cold extremities	
11			E		**E** S	I E	I					
12	I					E				Rectal discomfort		

*Subjects for whom the first experimental session was the saline condition.

†In instances in which like symptoms occurred both in epinephrine (E) and in saline (S) conditions, but were discernibly different in degree, bold face denotes greater severity of response.

were entirely congruent with earlier stress reactions. Some even confessed at this time that they had been less than frank during their first interview in admitting the many ways in which anxiety was customarily expressed. In a number of cases the symptoms withheld appeared to parallel those which emerged later under epinephrine. It is therefore not unlikely that the agreement obtained between epinephrine and initial interview data is actually diluted by the defensive reluctance of several subjects to acknowledge all of the ramifications of their ordinary anxiety reactions.

On the other hand, during the résumés following the experiment, all subjects claimed complete candor in having reported the effects of epinephrine. Viewing Table 1 in another manner, we may note that of the total 71 anxiety symptoms revealed in original interview, 18 failed to occur with epinephrine. Those appearing during the infusions were uniformly mild when compared with usual stress reactions. Considering the findings as a whole, it seems that the low dose of epinephrine employed did tend to reactivate idiosyncratic anxiety responses, although in limited magnitude and intensity.

Analysis of the clinical data offers further material of interest. There are suggestive indications that general lability of affect and types of ego defense also play a role in determining the manner and extent of epinephrine effects. Thus it is striking that certain subjects whose history and interview behavior revealed an openness for the easy experience and expression of affect readily perceived psychological and somatic responses with epinephrine. Conversely, others who were evaluated as constricted personalities tending to encapsulate emotion and suppress its emergence into consciousness showed less appreciable subjective changes. The issue is rather nicely illustrated in the cases of two contrasting subjects. One person, who failed to complete the experiment and hence is not included in the present series, gave a long history of labile anxiety. He described himself as "intense," "excitable," and "tending to feel most emotions very deeply." Events in the past, such as school examinations, criticism from peers and superiors, presentations before medical staff, and the assignment for overseas duty with Army occupation forces, had uniformly occasioned extreme apprehensiveness, nausea, alternating constipation and diarrhea, frequent urge to urinate, headache, and weakness. Even as he recited these anecdotes, the subject flushed and tensed visibly. He admitted, and it was evident, that mere recollection of these experiences served to rearouse disturbance. His experimental sequence involved the administration of epinephrine as the first condition. Three minutes after the introduction of this solution he blanched sharply and his eyes began to tear. Within the following two minutes there rapidly occurred severe trembling, labored breathing, nausea, chattering of teeth, cold extremities, faintness, and the verbal expression of extreme fright. At this point a switch-over to saline was made, and within six minutes the subject had returned to his previous resting state. Unknown to him, epinephrine was then reintroduced, and within three minutes the severe panic witnessed earlier recurred. The procedure was discontinued and arrangements made for this subject to return for additional testing two weeks later. On this occasion he was given saline throughout and, although he developed moderate apprehensiveness and some somatic signs, he was capable of completing the entire session, including the performance tasks. Epinephrine treatment was attempted the next day, and, as before, within five minutes following infusion intense fear and bodily concomitants appeared. It is quite clear that for this subject epinephrine had the unique capacity of triggering off a full-blown free anxiety reaction. Yet it is extraordinary that during all these instances of anxiety evocation there was a complete absence of any significant changes in the cardiovascular readings. Apparently, anxiety was expressed primarily in the

realms of conscious awareness and overt behavior, with blood pressure and pulse rate remaining relatively constant, although one should certainly expect that other physiological and biochemical indices not measured in the present study would reflect this profound response.

A quite opposite picture was presented by another subject, with a well-defended, rather rigid character structure. His review of traumatic life situations was intellectualized and delivered with detachment. In reciting a hazardous escape from a building that caught fire in the middle of the night, he was matter-of-fact and claimed to have been unconcerned throughout the entire affair. In fact, until it became evident that this person rarely communicated conscious affect to himself, the interviewer wondered whether the meagerness of his account was due to a deliberate guarding against the disclosure of personally relevant material. During the epinephrine session the subject smiled constantly and stoutly affirmed that he was comfortable and symptom-free, despite very marked rises in blood pressure and pulse rate. For a very brief interval he grudgingly conceded the perception of a slightly accented heart beat, only to disavow it later and maintain that it was probably a product of his imagination. His equanimity was the more remarkable since the magnitude of his pulse pressure was so extreme, rising at times to 105 mm. Hg, that termination by reason of medical contraindication was considered.

Consistent with his mechanism of denial, this person was the only subject who at the end of the experiment could not distinguish the epinephrine occasion. Even more revealing was the subsequent statement that he never really becomes aware of anxiety until integrated motor activity is impaired. Thus, for example, he only begins to recognize that he must be anxious when he develops a hand tremor in the course of executing a fine movement.

Cardiovascular Indices.—Epinephrine in the dosage employed produced a distinct physiological response in all subjects. In every instance pulse pressure increased, averaging 20 mm. Hg. On the whole, this effect was due both to a rise in systolic and to an equivalent fall in diastolic blood pressure. Yet wide individual differences obtained: Some persons had a systolic rise greatly in excess of their diastolic fall, while others showed an opposite trend. Similarly, with one exception, all subjects had elevations in pulse rate, the mean increase amounting to 13 beats per minute. These responses were usually discernible two to three minutes following the commencement of infusion, with an additional two to three minutes required before maximal change was realized. Pointing to the significance of these responses, however small in magnitude, was their persistence throughout the period of epinephrine administration and their prompt disappearance following termination of the infusion.

Performance Tests.—The results for the various repeated tests are shown in Table 2. Of these procedures, only the more clearly motor tasks were affected by epinephrine. Hand steadiness, physical persistence, and motor inhibition show a statistically significant decrease, steadiness at the <0.001 level of confidence and the others at the <0.05 and approximately the 0.05 levels, respectively. No reliable trends are apparent on the remaining tests in the battery. The suggestion, therefore, is one of diminished motor control under the influence of epinephrine, with the other functions sampled mainfesting no systematic changes.

Comment

Our concern in this study was twofold: (1) to determine the effects of continuous intravenous infusion of epinephrine at a low dose level on anxiety and its concomitants, and on selected measures of cardiovascular activity, sensory threshold, motor performance, and intellectual control; and (2) to determine whether and how personality factors were related to the subjective responses and patterns of symptoms pro-

TABLE 2.—*Mean Differences in Performance on Repeated Tests Under Epinephrine and Saline Conditions*

Procedure	Unit	Epinephrine	Saline	Differences	S.E.D	t	P
CFF: Trials 1–5, mean	Cps	24.02	24.17	−0.15	0.98	0.15	ns
CFF: Trials 6–10, mean	Cps	24.97	22.76	2.21	1.37	1.61	ns
CFF: Trials 11–15, mean	Cps	23.82	22.41	1.41	0.95	1.48	ns
CFF: Trials (1–5) ± (11–15), means	Cps	0.20	1.77	−1.57	1.36	1.15	ns
CFF: Trials 1–5, A.D.	Cps	1.03	1.27	−0.24	0.24	1.00	ns
CFF: Trials 6–10, A.D.	Cps	1.94	0.70	1.24	0.88	1.41	ns
CFF: Trials 11–15, A.D.	Cps	0.74	0.81	−0.07	0.12	0.58	ns
Hand steadiness	No. of contacts	60.3	28.7	31.6	4.9	6.45	<0.001
Motor persistence	Sec.	68.0	81.0	−13.0	5.0	2.60	<0.05
Motor inhibition	Sec.	242.4	284.5	−42.1	19.0	2.22	=0.05
Stroop task	Sec.	83.2	85.8	−2.6	2.6	1.00	ns
Memory for digits	Total score	13.2	13.1	0.1	0.6	0.01	ns
Word fluency	Sec.	94.2	112.3	−18.1	17.7	1.02	ns

duced. In pursuing the latter question, it was necessary first to demonstrate that the epinephrine employed induced changes over and above those developed by a neutral substance.

The results showed it to be the case. Epinephrine occasioned a limited, but quite consistent and continuing, elevation of blood pressure and pulse rate in all subjects. Among the performance tests, the three motor tasks revealed significant alterations reflecting a decrement in motor control, albeit the other procedures were not systematically influenced. In both frequency and intensity the subjective changes elicited by epinephrine exceeded those occurring with saline. However, whenever anxiety was experienced as a distinct conscious affect, it was of a low-grade order, expressed usually as a slight apprehensiveness or generalized uneasiness. Altogether, the findings indicate that epinephrine produced mild to moderate changes in emotional state and physiological and psychological functioning, although in certain instances particular subjects behaved more extremely.

These results, of course, must be evaluated in the light of our highly selected experimental population. Hospital interns were used because they constituted a relatively homogeneous group (at least with regard to age, health, occupation, and current environment) and because, by virtue of their medical sophistication, they could sensitively note and communicate their varied reactions. It remains for further research to ascertain whether other groups would display comparable effects.

Yet this does not in the least detract from the main import of the findings, namely, the correspondence of psychological and somatic changes perceived by each subject under epinephrine with those singularly typical of his reactions in previous situations of anxiety. The group exhibited a fairly wide range of symptoms under epinephrine, with sharp differences in number and type among subjects. However, those found in any given person tended to be consistent in locus and quality with the symptoms peculiar to him in ordinary life stresses. Thus, behavior evoked by exogenous epinephrine is continuous with the responses historically associated with the arousal of anxiety for the particular subject.

The nature of the psychological defenses with which the subject enters the experiment likewise appears to be related to the extent of response evoked by epinephrine. Tightly defended persons were less prone to experience subjective changes than persons who are habitually given to ready expression of affect. In the two illustrative cases chosen because of their extreme and contrasting emotional reactions to epinephrine, we have also noted a striking difference in cardiovascular response: The rigid subject who throughout remained unruffled and self-possessed showed profound alterations in blood pressure and pulse rate, whereas the labile subject who developed a state of panic had a surprising lack of change on these indices. We are more willing to conclude that personality characteristics affect the degree of emotional response, but at least from these two cases there is the provocative

suggestion that the apparent polarity in effects at a psychological level may have its counterpart in distinctive physiological reactions. In earlier studies of paratroop candidates undergoing the real life stress of airborne training, we have similarly encountered instances in which patterns of psychological and somatic functioning seemed to be associated with the character of the subject's defense mechanisms.[9]

Obviously, the relationships of specific predisposing personality traits and epinephrine response require more definitive experiment. We would not imply that type of defense is the only factor of moment. For it is logical to suppose that other issues are of consequence as well, for example, the adequacy of the defenses, quite apart from their nature, and, from a somatic standpoint, such likely factors as organ vulnerability. Such considerations would link the total appreciation of epinephrine effects with some of the major emphases in current psychosomatic research in which a stress response, whether induced by psychological, physical, or chemical agents, is evaluated in the light of enduring aspects of personality organization. The present exploratory study provides a valid basis for further inquiry in this problem area.

Summary

Twelve healthy medical interns were given prolonged intravenous epinephrine infusion at a low dose level (5γ/kg. body wt/hr.) and evaluated for changes in subjective state, cardiovascular activity, and a variety of tasks sampling sensory thresholds, motor performance, and intellectual control. The experimental design involved an initial clinical interview, which reviewed the subject's past history of stress response in terms of the arousal of conscious anxiety and perceived somatic concomitants, and two occasions of testing, placebo (control) and epinephrine, arranged in counterbalanced order. In all important respects a "double-blind" procedure was employed.

Pulse rate and pulse pressure were mild to moderately, yet consistently, elevated during the epinephrine state. Among the performance tests, only the motor tasks were significantly affected, indicating a decrease in motor control. Epinephrine symptoms were both more numerous and more pronounced than those produced with saline. The commonest subjective response was a perception of heightened heart rate and/or heart beat. More striking was a distinct tendency for epinephrine to elicit personally patterned symptoms consistent with the subject's earlier history of anxiety. It appeared that types of defense were also related to the development of symptoms, emotionally labile subjects being more predisposed toward symptom formation than rigid or constricted personalities. Two contrasting cases further suggested that these psychological opposites may yield quite distinctive physiological responses to epinephrine. It was proposed that the total effect of epinephrine requires consideration of the person's psychological defense structure and characteristic reactions to stress.

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Reserpine in the Postwithdrawal Rehabilitation of Adolescent Opiate Addicts

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Reserpine (Serpasil, Ciba brand) has been a helpful adjunct to the treatment of a variety of psychiatric conditions.[1] Along with its reported tranquilizing effect, it is said to improve readiness for treatment and/or pyschotherapeutic communications. This note reports an exploratory study of the efficacy of this drug in the postwithdrawal rehabilitation of male adolescent opiate addicts.

These patients have serious emotional problems.[2] Some of the prominent features noted in this group of patients for which reserpine is a plausible medication are resentment, suppressed hostility, dysphoria, and denial of need for treatment despite evident difficulties in living and overt psychiatric symptomatology. We wished to determine whether reserpine would "tranquilize" these patients and/or enhance their acceptance of the therapeutic program of the institution.

Control and experimental patients were selected randomly one month after withdrawal of opiates had been completed. The patients were given 1 mg. of the drug by mouth daily, at first in divided doses and later in a single dose. None of the observers (or the patients) knew whether any patient was receiving the medication or the placebo. Fourteen patients received reserpine, and thirteen patients received the placebo. Medication was administered from three to eight days. The patients were observed prior to, during, and after the period of medication.

Both the experimental and the control group accepted oral medication poorly. They were suspicious about the investigation and "cooperated" as much as they did only because of considerable encouragement by the nursing staff. As the study progressed, the control group accepted the medication no worse than at the beginning, but the experimental group found the medication progressively less acceptable.

Efficacy of the medication was poor. Only two subjects in the experimental group improved. One of them improved from the standpoint of the staff, who noted that he was less overtly aggressive and antagonistic towards the nursing staff and other patients. However, the patient considered himself to be worse off; he complained bitterly about the medication (see below). The other patient who improved was a hypomanic youth who had some insight into his hypomanic state and wished to be "slowed down." None of the patients in the control group showed any improvement.

Four patients were not affected by the medication. Ten of the subjects in the control group were not affected by receiving the placebo.

Deleterious effects were prominent. Nine patients became progressively worse while on the medication. As their symptoms (described below) became worse, these patients refused to continue with the medication despite the support and encouragement of the staff. Four of these patients, including the one case who was less overtly aggressive and antagonistic toward the nursing staff, were described by the nursing staff and by the patients themselves (in interviews with

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the psychiatrist observers) as increasingly lethargic, depressed, and apathetic. Three of these nine patients became tense and hostile. One of them became suspicious and referential without quite becoming psychotic. Two of these nine patients developed acute psychotic states. One of them, a schizophrenic who had made a "social improvement" from an earlier acute hebephreniccatatonic state, became bizarrely hypochrondriacal. He felt his body was rotting. He became hyperactive and restless and threatened to swim away (in the wintertime) from the island on which the hospital is located. He was certain he was being poisoned. His mood was depressed, and he threatened suicide. His facial expression was extraordinarily alert. Medication was stopped after two weeks. One week thereafter, the patient had recovered from this acute flare-up of his underlying schizophrenic process. The second patient who became psychotic described himself as "evil," that is, angry and irritable with everyone. He had visual hallucinations of a male friend, bizarre hypochondriacal symptoms referred to his head and stomach, and he withdrew increasingly from participation in hospital activities. After three and a half weeks, medication was discontinued. One week thereafter, he had returned to his "basal" state, in which he passively conformed to the hospital program, despite the blandness of his affect and isolation from meaningful personal relationships.

Some of the patients receiving the placebo medication also changed for the worse. One patient became overtly psychotic and was transferred to another hospital. His psychosis continued after the placebo was discontinued. This patient was committed to a state hospital. Two patients became increasingly depressed. This was not influenced by taking them off the placebo.

Comment

Barsa and Kline[3] describe three stages in the reserpine treatment of hospitalized psychotic patients: (*a*) a sedative period, (*b*) a turbulent period, and (*c*) an integrative period.

Statistical Summary

	Experimental Group $N=14$	Control Group $N=13$
*a*Improvement	1	0
*b*No effects	4	10
*c*Mixed effects	1	0
*d*Ill effects	8	3
c+*d* together	9 (64.3%)	3 (23.1%

$d=41.2\%$
$P=0.05$ (Fisher's exact test)

Of the 10 of our patients who had any response at all to the medication, 9 developed symptoms akin to the turbulent period described by these authors. For our patients, reserpine commonly seemed to uncover the pathologic anxiety and depression for which they had developed buttressing characterologic defenses. We might speculate that reserpine removes these defenses and leads the patient toward what might be called "acute psychic decompensation." If continued—or larger—doses of reserpine could be given regardless of the cooperation of the patient, this "turbulent" period might lead toward some kind of integration. However, in a rehabilitation center where the physician is, in large measure, dependent on the patient's cooperation, a regimen of enforced medication and control despite a "turbulent" response to the drug is not feasible.

In summary, our observations suggest that oral reserpine taken voluntarily is not a useful adjunct to the postwithdrawal rehabilitation of adolescent opiate addicts. It "tranquilized" only the exceptional case in our sample and did not enhance their acceptance of the therapeutic program of the institution. For our population, the modal response to the drug was deleterious.

The medication and placebo tablets were supplied to us by Ciba Pharmaceutical Products, Inc., Summit, N. J.

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Reliability of Mecholyl Test

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Introduction

Funkenstein and his collaborators, in a series of papers, described an autonomic nervous system test of prognostic significance in relation to electroshock. This test originally consisted of intravenous injection of epinephrine (adrenergic stimulation) and intramuscular injection of methacholine U. S. P. (Mecholyl) (cholinergic stimulation). Subsequently, it was found that the Mecholyl test alone predicted the results of the electroshock treatment at a better than $P=0.01$ level.* Mecholyl is a cholinergic drug, which when injected produces a fall of blood pressure, due to a peripheral action on the blood vessels. This may be followed by a rise in the blood pressure due to a homeostatic reaction of the higher hypothalamic sympathetic center (Gellhorn [5]).

Subjects, irrespective of their diagnosis, who react to injection of Mecholyl by a pronounced fall of the blood pressure respond to the electroshock therapy much better than subjects who respond by a rise of the blood pressure or only by a small fall. In view of the fact that blood pressure reaction to the Mecholyl test depends both on the peripheral action of the drug and on the activity of the autonomic centers in the hypothalamus (related to the hypothalamic sleep-wakefulness centers [Gellhorn [5]]), a hypothesis was postulated that there could be diurnal variation in the results of the Mecholyl test, corresponding to the level of the activity of the sleep-wakefulness centers in the hypothalamus or its vicinity.

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Procedure

To test this hypothesis, the Mecholyl test was administered, once in the morning and once in the evening, to 20 patients, 15 males and 5 females, varying in age from 18 to 58 (mean age, 33.1), and suffering from the following conditions:

Schizophrenia	4
Depressions	4
Psychopathic personality	3
Anxiety states	6
Epilepsy	1
Hyperchondriacal state	1
Hysteria	1

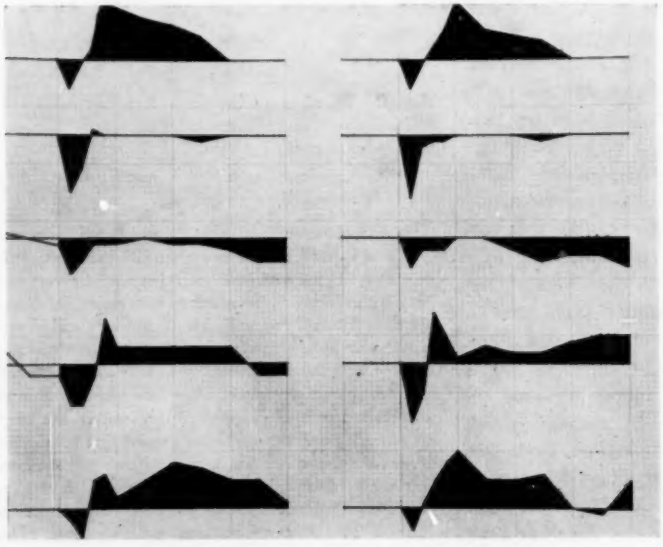
The test consisted of measuring blood pressure and pulse every 5 minutes for 20 minutes, followed by subcutaneous injection of 10 mg. of Mecholyl, followed by further measuring of blood pressure every 2 minutes for 10 minutes and every 5 minutes for 30 minutes. The results were recorded in a form of a graph. The change in the systolic blood pressure after the injection was determined in each patient by measuring the area above and below the curve, expressed by the number of small squares on the graph paper. All patients had their Mecholyl test in the morning at 9 a.m. and their evening test at 10 p.m. There was a 37-hour time interval between the two tests. The blood pressure was taken always from the same arm. The patients who were undergoing electroshock treatment or were on drugs affecting the autonomic nervous system (chlorpromazine and reserpine) were not included in the series. Ten patients had their first test in the morning and the second in the evening; with the other ten, the procedure was reversed, and the first test was administered in the evening and the second in the morning.

Results

The values for the mean rise of the blood pressure were 27.5 squares in the morning (S.D. 48.81) and 39.7 squares in

the evening (S.D. 55.07). The values for the mean fall of blood pressure were 77.15 squares in the morning (S.D. 81.87) and 80.65 squares in the evening (S.D. 62.85).

There was a change in the type of he reaction to the Mecholyl test in five patients: Three who reacted by a rise of the blood pressure in the morning reacted by a fall of the blood pressure in the evening. The other two reacted by a fall of the blood pressure in the morning and by a rise of the blood pressure in the evening. In the remaining 15 patients the type of the reaction remained unchanged. The difference between the numbers of the patients in the two groups is statistically significant ($0.05>p>0.01$. There was also a great consistency in the records of the patients who did not change the type of reaction. This consistency was measured by correlating the sizes of the areas of the rise and fall of the pressure in the morning and the areas of the rise and fall in the evening. Spearman's rank-difference correlation method was used. The correlation between the morning and the evening rise of the blood pressure was $\rho=0.82$ (S.E.$=0.09$). The correlation between the morning and evening falls was $\rho=0.9$ (S.D.$=0.05$). (These correlations are statistically valid, as they both are better than the 1% level). Moreover, the graphs showed a marked similarity between the profiles of the systolic blood pressure and pulse rate in the morning record and those in the evening record of the same person. There was an individual pattern in the reaction of the autonomic nervous system, which remained almost unchanged for 37 hours, and when it did change, it changed in stepwise fashion; the type of the reaction changed. In order to illustrate the individuality of the reaction pattern, the profiles of changes in the systolic blood pressure in five patients after a Mecholyl injection are reproduced. These are two records for each patient, representing his morning and his evening Mecholyl tests.



Profiles of the recordings of the systolic blood pressure after Mecholyl injections in five subjects. (Morning readings are recorded on the left side of the figure; evening readings, on the right side.)

The black areas above and below the basal line represent the rise and fall of the blood pressure after the Mecholyl injection. The basal line is the mean of the three readings of the systolic blood pressure before the Mecholyl injection. The areas of fall and rise of the blood pressure are measured in small squares. (Each square represents 2 mm. Hg each minute.)

Summary and Conclusions

There is no consistent diurnal variation in the Mecholyl test, although some subjects may change their type of reaction.

The Mecholyl test appears to be quite reliable in the majority of the subjects, and there is very little change between the results obtained in the first and those in

the second administration of the test, irrespective of the time of the day.

There is a suggestion that the reactivity of the autonomic nervous system may change in stepwise fashion.

The majority of the subjects show characteristic profiles, which remain the same on the subsequent tests.

Dr. D. G. McKerracher, Dr. A. Hoffer, and Dr. R. Fischer gave help and advice.

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Correspondence

DETAILS OF ELECTROSHOCK THERAPY

To the Editor: In the Washington area psychiatrists interested in electric shock therapy have been confronted with the same legal difficulties encountered by our colleagues in other cities. The malpractice situation here has become quite acute, and we are taking every step within our power to cope with the situation.

GEORGETOWN UNIVERSITY MEDICAL CENTER
OUT PATIENT DEPARTMENT

ELECTRO SHOCK TREATMENT CONSENT FORM

_____
(Date)

I _____ of

_____

being the _____ and nearest relative of
(Relationship)

_____ a patient in the Georgetown

University Hospital, Washington, D. C., do hereby authorize and direct

Dr. _____, or his designee, to administer

electroshock treatment, having been fully informed of its nature and purpose.

I also agree to hold the Georgetown University Hospital, all of its officers

and employees, and the attending physicians free from liability for any

injury, including fractures and dislocations, which may result from such

treatment.

_____
(Signed)

Witness:

_____
(Name)

Details of Electroshock Therapy

Electroshock therapy is an accepted form of treatment for certain types of nervous and mental illness. It has been used successfully in thousands of cases since its introduction in 1938. It is one of the most effective ways of treating depressed patients with suicidal tendencies or patients who might otherwise require prolonged hospitalization.

The psychiatrist himself gives the treatment, using a specially designed electronic instrument. The treatment consists of passing a controlled electric current between two electrodes applied to the patient's temples. In some instances, the patient may be given medication prior to treatment to reduce tension and produce muscular relaxation. The patient experiences no discomfort or pain during the treatment; he does not feel the electric current and has no memory of the treatment. When the treatment is given, the patient becomes immediately unconscious and has strong muscular contractions of a convulsive nature. These contractions last 35 to 50 seconds. Complete relaxation follows and several minutes later the patient gradually regains consciousness. His condition is similar to that of a patient emerging from brief anasthesia. Within 15 to 60 minutes, the confusion clears and the patient is able to recognize his surroundings. Following this, the patient is permitted to get up and about. Headache and nausea sometimes occur, but these are infrequent and usually respond rapidly to simple treatment.

The number of treatments in any given case will vary with the condition being treated, and the individual response to treatment. The frequency of treatment will also vary with each case. As the treatments progress (usually after the 3rd and 4th treatment), a certain amount of haziness of memory and confusion develops. This memory impairment is transitory and clears up within several weeks following the last treatment.

Electroshock therapy, like any other medical or surgical procedure involves a certain amount of calculated risk. Complications are infrequent, the most common being fractures and/or dislocations of the extremities, or fractures of the vertebrae. These may sometimes occur, in spite of all precautions and must be looked upon as a recognized hazard of the treatment. Should such an injury occur, the patient and his family will be notified and urged to call in a physician competent to treat the complication.

During the hospital treatment, the patient's general care is provided by the hospital personnel. On discharge from the hospital, the patient begins a "convalescent period" of several weeks duration during which he must be under strict supervision of some member of the family or some responsible person selected by the family. This precaution is necessary because of the temporary mental confusion and impairment of memory. During this entire period, the patient is not permitted to drive an automobile, to transact any business or to carry on his usual employment until the doctor gives his permission. He should not be permitted to leave the house unless accompanied by a responsible companion because of the possibility that he may wander off and get lost. Supervision is very important and must be provided by a responsible person.

Finally, a word about the results of treatment. Although the results in most cases are gratifying, not all cases will respond equally well. As in all forms of medical treatment in general, some patinets will recover promptly; others will recover only to relapse again and require further treatment; still others may fail to respond at all.

The above information has been prepared to answer some of the most frequently asked questions concerning electroshock therapy. The treating psychiatrist will be glad to answer any further questions which may occur to the patient or his family.

When the patient is treated by the ambulatory or outpatient method the family, or someone designated by the family, has definite and real responsibility for the patient's care. The patient is escorted to the hospital or the doctor's office. The responsible person stays with the patient until he reacts from the treatment and then escorts him back home. During the approximately two-week period of treatment and for at least two or three weeks following termination of treatment the patient must be under the strict supervision and companionship of the family.

Date:.....

I, ..., hereby acknowledge receipt and understanding of this information sheet which contains details relative to the care, risks, and treatment to be received by

.....

Witness:.....**Signed:**.....

One of the local problems has been the legal question regarding the matter of acquainting the family and the patient with all the possible complications of electric shock therapy. In order to attempt to offset this specific aspect of the problem, our local group has developed the enclosed information sheet which we furnish to the family and patients who are candidates for electric shock therapy. As can be seen, there is provision for the patient or a responsible member of the family to sign a receipt indicating that he understands the details. In addition, we insist that the family keep a copy for future reference. This information sheet is used as an adjunct to our regular consent form authorizing us to administer the treatment.

ISADORE RODIS, M.D.
ROBERT H. GROH, M.D.
Washington, D. C.

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